

10/609,298

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prophetic substances  
NEWS 4 JAN 28 USPATFULL, USPAT2, and USPATOLD enhanced with new  
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NEWS 5 JAN 28 MARPAT searching enhanced  
NEWS 6 JAN 28 USGENE now provides USPTO sequence data within 3 days  
of publication  
NEWS 7 JAN 28 TOXCENTER enhanced with reloaded MEDLINE segment  
NEWS 8 JAN 28 MEDLINE and LMEDLINE reloaded with enhancements  
NEWS 9 FEB 08 STN Express, Version 8.3, now available  
NEWS 10 FEB 20 PCI now available as a replacement to DPCI  
NEWS 11 FEB 25 IFIREF reloaded with enhancements  
NEWS 12 FEB 25 IMSPRODUCT reloaded with enhancements  
NEWS 13 FEB 29 WPINDEX/WPIDS/WPIX enhanced with ECLA and current  
U.S. National Patent Classification  
NEWS 14 MAR 31 IFICDB, IFIPAT, and IFIUDB enhanced with new custom  
IPC display formats  
NEWS 15 MAR 31 CAS REGISTRY enhanced with additional experimental  
spectra  
NEWS 16 MAR 31 CA/CAPLUS and CASREACT patent number format for U.S.  
applications updated  
NEWS 17 MAR 31 LPCI now available as a replacement to LDPCI  
NEWS 18 MAR 31 EMBASE, EMBAL, and LEMBASE reloaded with enhancements  
NEWS 19 APR 04 STN AnaVist, Version 1, to be discontinued  
NEWS 20 APR 15 WPIDS, WPINDEX, and WPIX enhanced with new  
predefined hit display formats  
NEWS 21 APR 28 EMBASE Controlled Term thesaurus enhanced  
NEWS 22 APR 28 IMSRESEARCH reloaded with enhancements  
NEWS 23 MAY 30 INPAFAMDB now available on STN for patent family  
searching  
NEWS 24 MAY 30 DGENE, PCTGEN, and USGENE enhanced with new homology  
sequence search option  
NEWS 25 JUN 06 EPFULL enhanced with 260,000 English abstracts  
NEWS 26 JUN 06 KOREAPAT updated with 41,000 documents  
  
NEWS EXPRESS FEBRUARY 08 CURRENT WINDOWS VERSION IS V8.3,  
AND CURRENT DISCOVER FILE IS DATED 20 FEBRUARY 2008  
  
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NEWS IPC8 For general information regarding STN implementation of IPC 8

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FILE 'HOME' ENTERED AT 18:07:49 ON 08 JUN 2008

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=> file reg	SINCE FILE	TOTAL
COST IN U.S. DOLLARS	ENTRY	SESSION
FULL ESTIMATED COST	0.21	0.21

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STRUCTURE FILE UPDATES: 6 JUN 2008 HIGHEST RN 1026208-38-7  
DICTIONARY FILE UPDATES: 6 JUN 2008 HIGHEST RN 1026208-38-7

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=>  
Uploading C:\Program Files\Stnexp\Queries\10609298a.str

L1 STRUCTURE UPLOADED

=> d l1  
L1 HAS NO ANSWERS  
L1 STR

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

Structure attributes must be viewed using STN Express query preparation.

=> s l1  
SAMPLE SEARCH INITIATED 18:08:35 FILE 'REGISTRY'  
SAMPLE SCREEN SEARCH COMPLETED - 2232 TO ITERATE

89.6% PROCESSED	2000 ITERATIONS	24 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)		
SEARCH TIME: 00.00.01		

FULL FILE PROJECTIONS:	ONLINE	**COMPLETE**
	BATCH	**COMPLETE**
PROJECTED ITERATIONS:	41806 TO	47474
PROJECTED ANSWERS:	225 TO	845

L2 24 SEA SSS SAM L1

=> s l1 full  
FULL SEARCH INITIATED 18:08:41 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED - 44523 TO ITERATE

100.0% PROCESSED	44523 ITERATIONS	519 ANSWERS
SEARCH TIME: 00.00.01		

L3 519 SEA SSS FUL L1

=> file caplus	SINCE FILE	TOTAL
COST IN U.S. DOLLARS	ENTRY	SESSION
FULL ESTIMATED COST	178.36	178.57

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FILE 'CAPLUS' ENTERED AT 18:08:46 ON 08 JUN 2008  
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FILE COVERS 1907 - 8 Jun 2008 VOL 148 ISS 24  
FILE LAST UPDATED: 6 Jun 2008 (20080606/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/legal/infopolicy.html>

=> s 13

L4 120 L3

=> s 14 and flavivirus or pestivirus or flaviviridae or hcv or hepatitis c

1747 FLAVIVIRUS

864 FLAVIVIRUSES

2025 FLAVIVIRUS

(FLAVIVIRUS OR FLAVIVIRUSES)

501 PESTIVIRUS

266 PESTIVIRUSES

597 PESTIVIRUS

(PESTIVIRUS OR PESTIVIRUSES)

645 FLAVIVIRIDAE

14183 HCV

24 HCVS

14187 HCV

(HCV OR HCVS)

67218 HEPATITIS

1 HEPATITISES

67218 HEPATITIS

(HEPATITIS OR HEPATITISES)

3835463 C

20967 HEPATITIS C

(HEPATITIS(W)C)

L5 22498 L4 AND FLAVIVIRUS OR PESTIVIRUS OR FLAVIVIRIDAE OR HCV OR HEPATITIS C

=> s 14 and (flavivirus or pestivirus or flaviviridae or hcv or hepatitis c)

1747 FLAVIVIRUS

864 FLAVIVIRUSES

2025 FLAVIVIRUS

(FLAVIVIRUS OR FLAVIVIRUSES)

501 PESTIVIRUS

266 PESTIVIRUSES

597 PESTIVIRUS

(PESTIVIRUS OR PESTIVIRUSES)

645 FLAVIVIRIDAE

14183 HCV

24 HCVS

14187 HCV

(HCV OR HCVS)

67218 HEPATITIS

1 HEPATITISES

67218 HEPATITIS

(HEPATITIS OR HEPATITISES)

3835463 C

20967 HEPATITIS C

(HEPATITIS(W)C)

L6 58 L4 AND (FLAVIVIRUS OR PESTIVIRUS OR FLAVIVIRIDAE OR HCV OR HEPATITIS C)

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ITIS C)

=&gt; d bib abs hitstr 40-58 16

L6 ANSWER 40 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN  
 AN 2006:103884 CAPLUS  
 DN 144:171198  
 TI Preparation of alkyl-substituted 2-deoxy-2-fluoro-D-ribofuranosyl  
 pyrimidine and purine nucleoside analogs via condensation of the lactone  
 to nucleosides as potential antiviral agents  
 IN Wang, Peiyuan; Stec, Wojciech; Clark, Jeremy; Chun, Byoung-Kwon; Shi,  
 Junxing; Du, Jinfa  
 PA Pharmasset, Inc., USA  
 SO PCT Int. Appl., 34 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006012440	A2	20060202	WO 2005-US25916	20050721
	WO 2006012440	A3	20060727		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
	RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	AU 2005267051	A1	20060202	AU 2005-267051	20050721
	CA 2574651	A1	20060202	CA 2005-2574651	20050721
	EP 1773856	A2	20070418	EP 2005-775359	20050721
	R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR			
	CN 101023094	A	20070822	CN 2005-80031530	20050721
	BR 2005012104	A	20080311	BR 2005-12104	20050721
	JP 2008507547	T	20080313	JP 2007-522763	20050721
	US 20060199783	A1	20060907	US 2006-353597	20060213
	MX 200700803	A	20070402	MX 2007-803	20070119
	IN 2007KN00605	A	20070706	IN 2007-KN605	20070220
	KR 2007114344	A	20071203	KR 2007-703980	20070220
PRAI	US 2004-589866P	P	20040721		
	US 2004-608320P	P	20040909		
	US 2005-185988	A1	20050721		
	WO 2005-US25916	W	20050721		
OS	MARPAT 144:171198				
GI					

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB A process for preparing of 2-deoxy-2-fluoro-2-methyl-D-ribonolactones, I, wherein R1 and R2 can independently be H, CH3, acetyl, benzoyl, pivaloyl, 4-nitrobenzoyl, 3-nitrobenzoyl, 2-nitrobenzoyl, 4-chlorobenzoyl, 3-chlorobenzoyl, 2-chlorobenzoyl, 4-methylbenzoyl, 3-methylbenzoyl, 2-methylbenzoyl, 4-phenylbenzoyl, benzyl, 4-methoxybenzyl, trityl, trialkylsilyl, t-butyl-dialkylsilyl, t-butyl-diphenylsilyl, TIPDS, THP, MOM, or MEM are prepared and used in the condensation to 2-deoxy-2-fluoro-D-ribofuranosyl pyrimidine and purine nucleoside analogs. Thus, 2-deoxy-2-fluoro-D-ribofuranosyl pyrimidine and purine nucleoside analogs II and III, wherein X is a halogen; Y is N or CH; Z is a halogen, hydroxyl, ether, thiol, thioether, (un)substituted amine or alkyl; R1' is alkyl, vinyl, ethynyl; R2' and R3' can be same or different H, alkyl, arylalkyl, acyl, cyclic acetal such as 2',3'-O-isopropylidene or 2',3'-O-benzylidene, or 2',3'-cyclic carbonate; R4, R5, and R6 are independently H, halogen, hydroxyl, ether, thiol, thioether, N3,

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(un)substituted amine, (un)substituted amido, alkyl, halogenated alkyl, alkenyl, halogenated alkenyl, alkynyl, halogenated alkynyl, hydroxy alkyl, alkoxy are prepared and are potential anti-HCV agents. Specifically, IV was prepared (no yield, claimed) via condensation, alkylation and stereoselective fluorination reactions and can exhibit potential use as an anti-HCV agent.

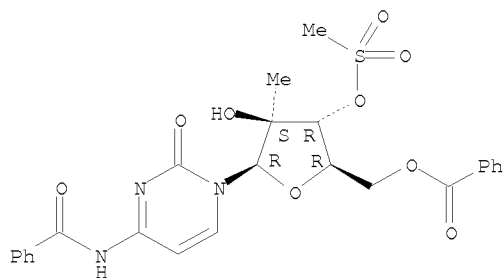
IT 874638-81-0P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of alkyl-substituted 2-deoxy-2-fluoro-D-ribofuranosyl pyrimidine and purine nucleoside analogs via condensation of the lactone to nucleosides)

RN 874638-81-0 CAPLUS

CN Benzamide, N-[1-[5-O-benzoyl-2-C-methyl-3-O-(methylsulfonyl)- $\beta$ -D-arabinofuranosyl]-1,2-dihydro-2-oxo-4-pyrimidinyl]- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 41 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2005:1151389 CAPLUS

DN 145:271979

TI NM 283, an efficient prodrug of the potent anti-HCV agent 2'-C-methylcytidine

AU Pierra, C.; Benzaria, S.; Amador, A.; Moussa, A.; Mathieu, S.; Storer, R.; Gosselin, G.

CS Laboratoire Cooperatif Idenix, CNRS, Universite Montpellier II, Montpellier, 5, Fr.

SO Nucleosides, Nucleotides & Nucleic Acids (2005), 24(5-7), 767-770  
CODEN: NNNAFY; ISSN: 1525-7770

PB Taylor & Francis, Inc.

DT Journal

LA English

OS CASREACT 145:271979

AB In order to improve the oral bioavailability of 2'-C-methylcytidine, a potent anti-HCV agent, the corresponding 3'-O-L-valinyl ester derivative (NM 283) has been synthesized. Based on its ease of synthesis and its physicochem. properties, NM 283 has emerged as a promising antiviral drug for treatment of chronic HCV infection.

IT 23643-36-9P 31448-54-1P 640725-70-8P  
642075-42-1P

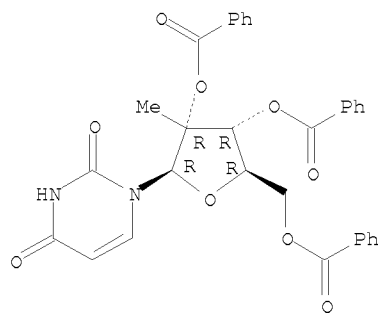
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of NM 283 as efficient prodrug of potent anti-HCV agent 2'-C-methylcytidine)

RN 23643-36-9 CAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-(2,3,5-tri-O-benzoyl-2-C-methyl- $\beta$ -D-ribofuranosyl)- (9CI) (CA INDEX NAME)

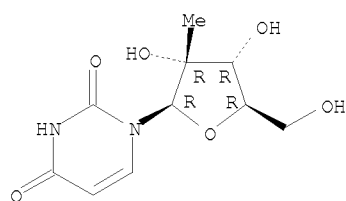
Absolute stereochemistry.

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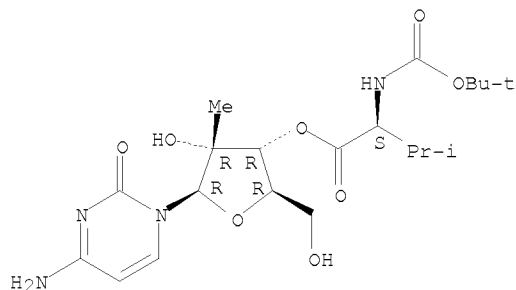
RN 31448-54-1 CAPLUS  
CN Uridine, 2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



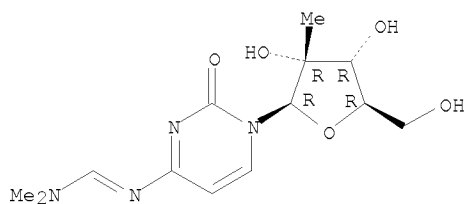
RN 640725-70-8 CAPLUS  
CN L-Valine, N-[(1,1-dimethylethoxy)carbonyl]-, 3'-ester with  
2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry.



RN 642075-42-1 CAPLUS  
CN Cytidine, N-[(dimethylamino)methylene]-2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry unknown.



IT 20724-73-6P  
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);  
BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);

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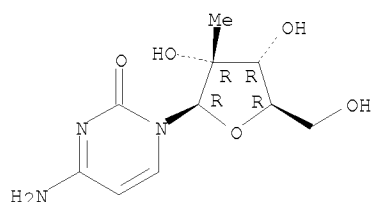
USES (Uses)

(preparation of NM 283 as efficient prodrug of potent anti-HCV agent 2'-C-methylcytidine)

RN 20724-73-6 CAPLUS

CN Cytidine, 2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry.



IT 640725-71-9P

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use);

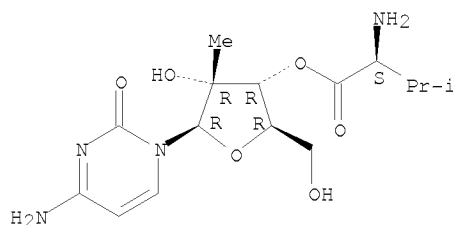
BIOL (Biological study); PREP (Preparation); USES (Uses)

(prodrug; preparation of NM 283 as efficient prodrug of potent anti-HCV agent 2'-C-methylcytidine)

RN 640725-71-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



● 2 HCl

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 42 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2005:684531 CAPLUS

DN 143:431740

TI Emerging drugs for chronic hepatitis C

AU Bhopale, Girish Mahadeorao; Nanda, Rabindra Kumar

CS Research and Development Division, Hindustan Antibiotics Limited, Pimpri, Pune, 411018, India

SO Hepatology Research (2005), 32(3), 146-153

CODEN: HPRSFM; ISSN: 1386-6346

PB Elsevier B.V.

DT Journal; General Review

LA English

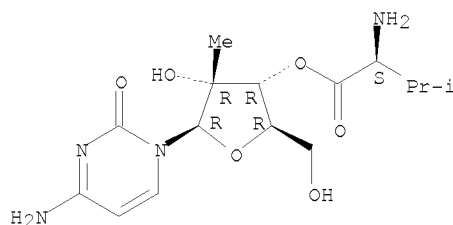
AB A review. Hepatitis C virus (HCV) is a major cause of chronic hepatitis, liver cirrhosis and hepatocellular carcinoma worldwide. A combination therapy comprising pegylated interferon and ribavirin currently represents the most effective therapy for chronic HCV infection. The limitations of this current therapy mainly its efficacy and significant side effects have prompted the development of new drugs. Few categories of therapeutic agents appear promising for future therapy, e.g. novel interferons, ribavirin analogs, antisense oligonucleotides, short interfering RNAs, ribozymes, enzyme inhibitors, immunomodulatory agents, antifibrotic agents, therapeutic vaccines and antibodies. Few drugs belong to afore-mentioned categories have already reached the different clin. phases of development. The

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present article highlights the status of current available therapies and emerging drugs for the treatment of hepatitis C.

IT 640725-71-9, NM 283  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (NM283 proved promising therapeutic effect in treating chronic hepatitis C patient)  
 RN 640725-71-9 CAPLUS  
 CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



● 2 HCl

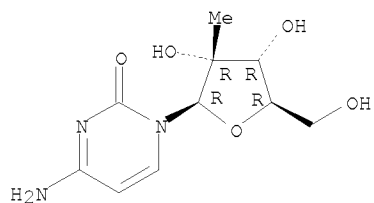
RE.CNT 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 43 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN  
 AN 2005:648160 CAPLUS  
 DN 143:248607  
 TI Design, Synthesis, and Antiviral Activity of 2'-Deoxy-2'-fluoro-2'-C-methyl-cytidine, a Potent Inhibitor of Hepatitis C Virus Replication  
 AU Clark, Jeremy L.; Hollecker, Laurent; Mason, J. Christian; Stuyver, Lieven J.; Tharnish, Phillip M.; Lostia, Stefania; McBrayer, Tamara R.; Schinazi, Raymond F.; Watanabe, Kyoichi A.; Otto, Michael J.; Furman, Phillip A.; Stec, Wojciech J.; Patterson, Steven E.; Pankiewicz, Krzysztof W.  
 CS Pharmasset, Inc., Princeton, NJ, 08540, USA  
 SO Journal of Medicinal Chemistry (2005), 48(17), 5504-5508  
 CODEN: JMCMAR; ISSN: 0022-2623  
 PB American Chemical Society  
 DT Journal  
 LA English  
 OS CASREACT 143:248607  
 AB The pyrimidine nucleoside-  $\beta$ -D-2'-deoxy-2'-fluoro-2'-C-methylcytidine (I) was designed as a hepatitis C virus RNA-dependent RNA polymerase (HCV RdRp) inhibitor. The title compound was obtained by a DAST fluorination of N4-benzoyl-1-(2-methyl-3,5-di-O-benzoyl- $\beta$ -D-arabinofuranosyl)cytosine to provide N4-benzoyl-1-(2-fluoro-2-methyl-3,5-di-O-benzoyl- $\beta$ -D-ribofuranosyl)cytosine. The protected 2'-C-methylcytidine was obtained as a byproduct from the DAST fluorination and allowed for the preparation of two biol. active compds. from a common precursor. Compound I and 2'-C-methylcytidine were assayed in a sub-genomic HCV replicon assay system and found to be potent and selective inhibitors of HCV replication. Compd.I shows increased inhibitory activity in the HCV replicon assay compared to 2'-C-methylcytidine and low cellular toxicity.  
 IT 20724-73-6  
 RL: PAC (Pharmacological activity); BIOL (Biological study)  
 (design, synthesis via fluorination, and antiviral activity of 2'-deoxy-2'-fluoro-2'-C-methyl-cytidine, a potent inhibitor of Hepatitis C virus replication)  
 RN 20724-73-6 CAPLUS  
 CN Cytidine, 2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry.

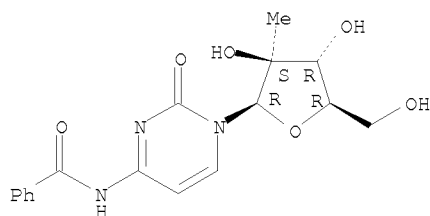


10/609,298



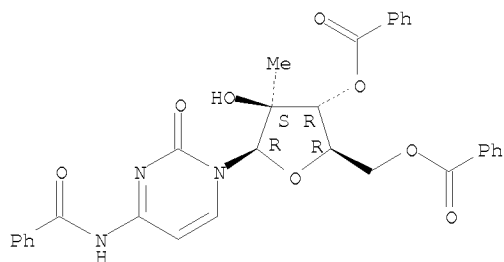
IT 817204-35-6P 863329-62-8P 863329-64-0P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(design, synthesis via fluorination, and antiviral activity of  
2'-deoxy-2'-fluoro-2'-C-methyl-cytidine, a potent inhibitor of  
Hepatitis C virus replication)  
RN 817204-35-6 CAPLUS  
CN Benzamide, N-[1,2-dihydro-1-(2-C-methyl-β-D-arabinofuranosyl)-2-oxo-4-  
pyrimidinyl]- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



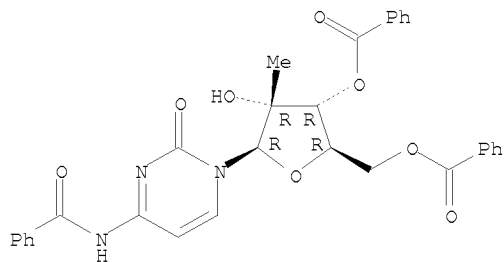
RN 863329-62-8 CAPLUS  
CN Benzamide, N-[1-(3,5-di-O-benzoyl-2-C-methyl-β-D-arabinofuranosyl)-  
1,2-dihydro-2-oxo-4-pyrimidinyl]- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 863329-64-0 CAPLUS  
CN Cytidine, N-benzoyl-2'-C-methyl-, 3',5'-dibenzoate (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

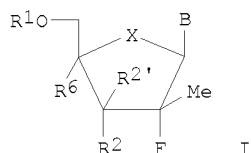


RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L6 ANSWER 44 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN  
 AN 2005:34765 CAPLUS  
 DN 142:94074  
 TI Preparation of modified fluorinated (2'R)-2'-deoxy-2'-fluoro-2'-C-methyl  
 nucleoside analogs as antiviral agents  
 IN Clark, Jeremy  
 PA Pharmasset, Ltd., Barbados  
 SO PCT Int. Appl., 228 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 2005003147	A2	20050113	WO 2004-US12472	20040421	
	WO 2005003147	A3	20050303			
	W:			AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW		
	RW:			BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG		
	AU 2004253860	A2	20050113	AU 2004-253860	20040421	
	AU 2004253860	A1	20050113			
	CA 2527657	A1	20050113	CA 2004-2527657	20040421	
	US 20050009737	A1	20050113	US 2004-828753	20040421	
	EP 1633766	A2	20060315	EP 2004-775900	20040421	
	R:			AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR		
	BR 2004010846	A	20060627	BR 2004-10846	20040421	
	CN 1816558	A	20060809	CN 2004-80019148	20040421	
	JP 2006526629	T	20061124	JP 2006-513231	20040421	
	MX 2005PA12788	A	20060222	MX 2005-PA12788	20051125	
	IN 2005DN06087	A	20080509	IN 2005-DN6087	20051227	
	NO 2005006221	A	20051228	NO 2005-6221	20051228	
	US 20080070861	A1	20080320	US 2007-854218	20070912	
PRAI	US 2003-474368P	P	20030530			
	US 2004-828753	A3	20040421			
	WO 2004-US12472	W	20040421			
OS	MARPAT 142:94074					
GI						



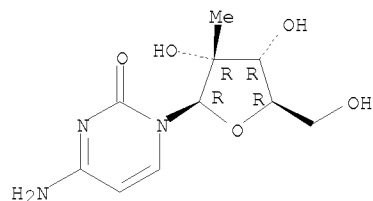
AB The disclosed invention provides nucleoside analogs I, wherein B is purine and pyrimidine nucleobase; X is O, S, CH<sub>2</sub>, Se, NH, N-alkyl, CHW, C(W)<sub>2</sub>; W is F, Cl, Br, iodo; R<sub>1</sub> is H, phosphate, H-phosphonate, acyl, Ph, alkyl, carboxyalkylamino, sulfonate ester, peptide, amino acid, sugar residue; R<sub>2</sub> and R<sub>2</sub>' are independently H, alkyl, alkenyl, alkynyl, vanyl, N<sub>3</sub>, CN, halogen, NO<sub>2</sub>, ester, alkoxy, thioalkyl, sulfoxide, sulfonyl; R<sub>6</sub> is alkyl, CN, Me, OMe, OEt, CH<sub>2</sub>OH, CH<sub>2</sub>F, N<sub>3</sub>, CHCN, CH<sub>2</sub>N<sub>3</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NHMe, CH<sub>2</sub>NMe<sub>2</sub>, alkylne; and methods of treating a Flaviviridae infection, including hepatitis C virus, West Nile Virus, yellow fever virus, and a rhinovirus infection in a host, including animals, and especially human, using a (2'R)-2'-deoxy-2'-fluoro-2'-C-Me nucleosides, or a pharmaceutically acceptable salt or prodrug thereof. Thus, (2'R)-2'-deoxy-2'-fluoro-2'-C-methylcytidine was prepared and tested as antiviral agent. The effects the nucleoside analogs tested on human bone

10/609,298

marrow cells are reported. (2'R)-2'-deoxy-2'-fluoro-2'-C-methylcytidine shows activity against Rhinovirus, West Nile virus, Yellow Fever virus, and Dengue virus. Cytotoxicity and effect of nucleoside analogs on human bone marrow cells are reported.

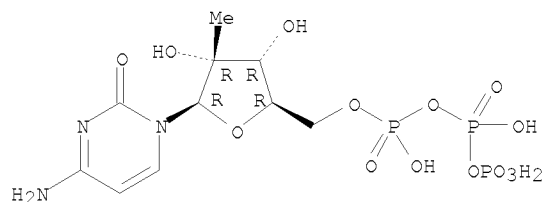
IT 20724-73-6 374750-28-4  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(preparation of modified fluorinated (2'R)-2'-deoxy-2'-fluoro-2'-C-Me nucleoside analogs as antiviral agents)  
RN 20724-73-6 CAPLUS  
CN Cytidine, 2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry.



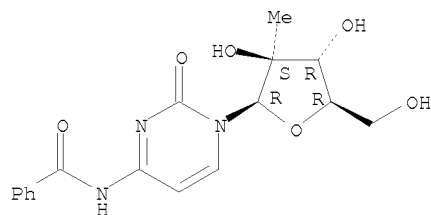
RN 374750-28-4 CAPLUS  
CN Cytidine 5'-(tetrahydrogen triphosphate), 2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry.



IT 817204-35-6P 817204-36-7P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of modified fluorinated (2'R)-2'-deoxy-2'-fluoro-2'-C-Me nucleoside analogs as antiviral agents)  
RN 817204-35-6 CAPLUS  
CN Benzamide, N-[1,2-dihydro-1-(2-C-methyl-β-D-arabinofuranosyl)-2-oxo-4-pyrimidinyl]- (CA INDEX NAME)

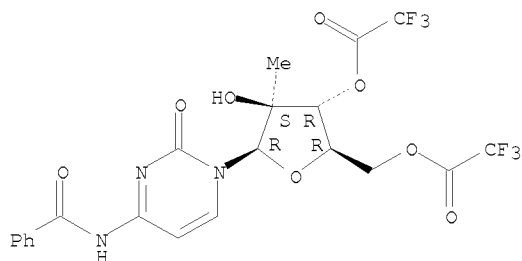
Absolute stereochemistry. Rotation (+).



RN 817204-36-7 CAPLUS  
CN Benzamide, N-[1,2-dihydro-1-[2-C-methyl-3,5-bis-O-(trifluoroacetyl)-β-D-arabinofuranosyl]-2-oxo-4-pyrimidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

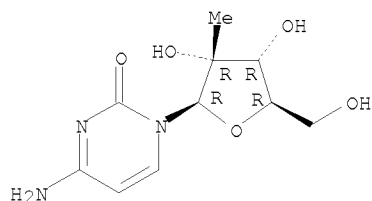
McIntosh



L6 ANSWER 45 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN  
 AN 2004:817630 CAPLUS  
 DN 141:307495  
 TI Use of nucleoside compounds and PALA for the treatment of  
 flaviviridae infections  
 IN Stuyver, Lieven J.  
 PA Pharmasset Ltd., Barbados  
 SO PCT Int. Appl., 120 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

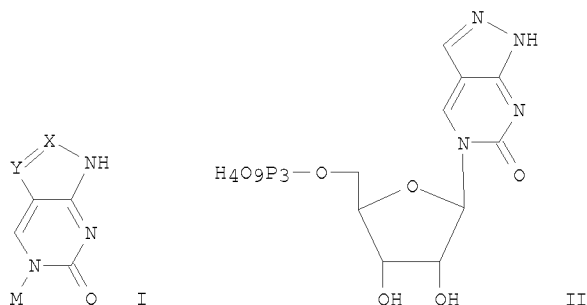
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004084796	A2	20041007	WO 2004-IB1429	20040329
WO 2004084796	A3	20060406		
W:				
AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW:				
BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004224575	A1	20041007	AU 2004-224575	20040329
CA 2529311	A1	20041007	CA 2004-2529311	20040329
US 20050049204	A1	20050303	US 2004-812448	20040329
EP 1626692	A2	20060222	EP 2004-724085	20040329
R:				
AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
BR 2004008846	A	20060704	BR 2004-8846	20040329
JP 2006524227	T	20061026	JP 2006-506588	20040329
CN 1980678	A	20070613	CN 2004-80011746	20040329
MX 2005PA10419	A	20060531	MX 2005-PA10419	20050928
PRAI US 2003-458635P	P	20030328		
WO 2004-IB1429	W	20040329		
OS MARPAT 141:307495				
AB				
The invention discloses a composition for and a method of treating Flaviviridae infections, e.g. bovine viral diarrhea virus, dengue Virus, West Nile virus, and hepatitis C virus, as well as abnormal cellular proliferation, in a host, including animals, and especially humans, using a nucleoside compound (Markush included) or N-(phosphonoacetyl)-L-aspartate (PALA), or a pharmaceutically acceptable salt or prodrug thereof.				
IT 20724-73-6				
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)				
(nucleoside compds. and PALA for treatment of flaviviridae infections)				
RN 20724-73-6 CAPLUS				
CN Cytidine, 2'-C-methyl- (CA INDEX NAME)				

Absolute stereochemistry.



L6 ANSWER 46 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN  
 AN 2004:780543 CAPLUS  
 DN 141:296247  
 TI Preparation of cytidine nucleoside analogs as antiviral agents  
 IN Girardet, Jean-Luc; Koh, Yung-Hyo; An, Haoyun; Hong, Zhi  
 PA Ribapharm Inc., USA  
 SO PCT Int. Appl., 59 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004080466	A1	20040923	WO 2003-US6992	20030307
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003225705	A1	20040930	AU 2003-225705	20030307
PRAI WO 2003-US6992	A	20030307		
OS MARPAT 141:296247				
GI				



AB Cytidine analogs I, wherein -X=Y- is -N=N-, -CH=N-, -N=CZ- or -CH=CZ-, wherein Z is H, halogen, or alkyl, and wherein M is a sugar or sugar analog; wherein the compound has a D-configuration or an L-configuration; with the proviso that where M is a substituted sugar with a ribofuranose ring having a heteroatom and substituents R1 and R2 on the C3'-atom, R3 and R4 on the C2'-atom, and R5 on the C5'-atom, R1-R4 together are not independently H, OH, F, NH2, N3, O-hydrocarbyl, or a reporter moiety, when the heteroatom is O, S, Se, SO, N-alkyl, or CH2, and when R5 is OH, SH, NH2, monophosphate, diphosphate, triphosphate, thiophosphate, or boranophosphate; and with the further proviso that M does not comprise a cyclopropenyl group, a morpholino group, or M is not a phosphonylmethoxyethyl, their prodrugs and/or metabolites are employed as pharmaceutically active compds. for treatment of diseases responsive to such compds. Particularly preferred diseases include viral diseases (e.g., HCV infection) and neoplasms (no biol. data). Thus

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nucleoside analog II was prepared and tested as antiviral agent. The virus is an HCV virus, an HIV virus, an RSV virus, an influenza virus, or a an HBV virus.

IT 23643-36-9

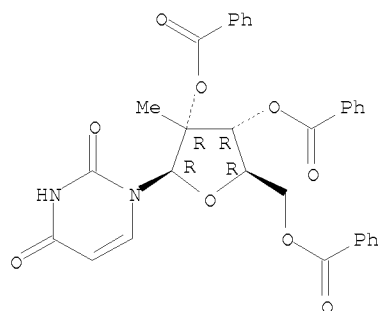
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of cytidine nucleoside analogs as antiviral agents)

RN 23643-36-9 CAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-(2,3,5-tri-O-benzoyl-2-C-methyl- $\beta$ -D-ribofuranosyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 760965-52-4P 760965-53-5P 760965-55-7P

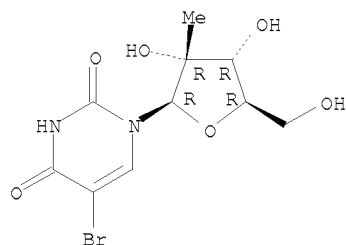
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of cytidine nucleoside analogs as antiviral agents)

RN 760965-52-4 CAPLUS

CN Uridine, 5-bromo-2'-C-methyl- (9CI) (CA INDEX NAME)

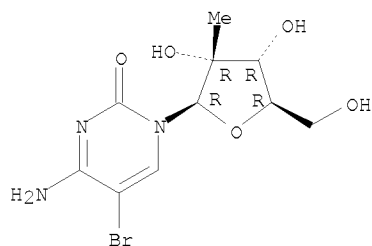
Absolute stereochemistry.



RN 760965-53-5 CAPLUS

CN Cytidine, 5-bromo-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

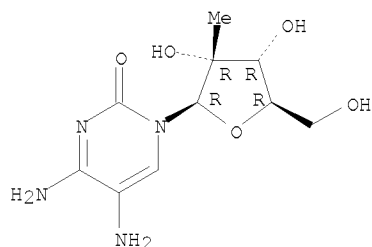


RN 760965-55-7 CAPLUS

CN Cytidine, 5-amino-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

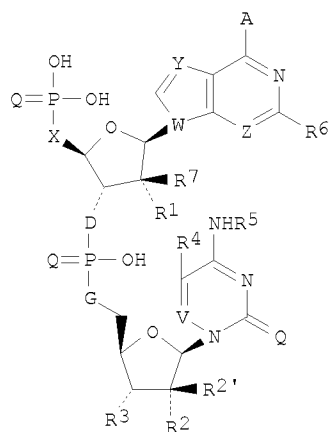
McIntosh



RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 47 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN  
AN 2004:652668 CAPLUS  
DN 141:167739  
TI Diribonucleotides as specific viral RNA-polymerase inhibitors for the  
treatment or prevention of viral infections  
IN Wu, Jim Zhen; An, Haoyun; Hong, Zhi  
PA USA  
SO U.S. Pat. Appl. Publ., 12 pp.  
CODEN: USXXCO  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 20040158054	A1	20040812	US 2003-360218	20030207
PRAI	US 2003-360218		20030207		
OS	MARPAT 141:167739				
GI					



I

AB The invention discloses compds. and methods using dinucleotide compds. I  
(A = H, OR, SR, NH<sub>2</sub>, or NHR; Q = O or S; V, W, Y, and Z = CH or N; X = O,  
S, NR, etc.; D and G = null, CH<sub>2</sub>, O, etc.; R<sub>1</sub>, R<sub>2</sub>, R<sub>2</sub>', R<sub>3</sub> = H, OR,  
halogen, CF<sub>3</sub> etc.; R<sub>4</sub> = R; R<sub>5</sub> = H, NH<sub>2</sub>, NHR, etc.; R<sub>6</sub> = H, NH<sub>2</sub>, NHCOR,  
etc.; R<sub>7</sub> = H, OR, SR, halogen, etc.; R = H, (un)substituted alkyl, aryl,  
etc.) comprising a first and second nucleoside. The dinucleotide inhibits  
viral RNA polymerase and at least one of the nucleosides exhibits  
antiviral activity when cleaved from the dinucleotide.

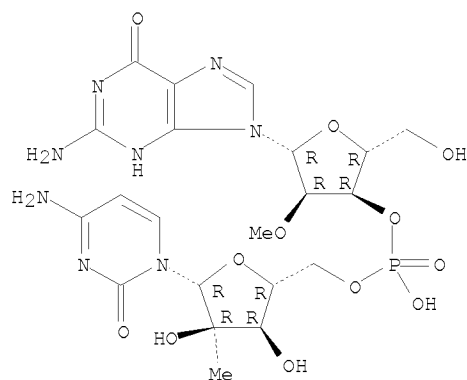
IT 735268-87-8P  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
(Uses)  
(diribonucleotides as specific viral RNA-polymerase inhibitors for  
treatment or prevention of viral infections)

RN 735268-87-8 CAPLUS

10/609,298

CN Cytidine, 2'-O-methylguanylyl-(3'→5')-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 735268-88-9

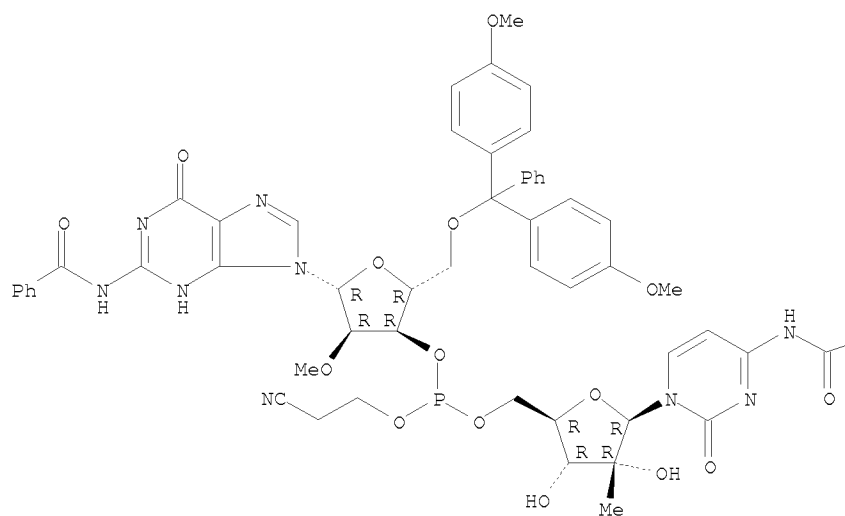
RL: RCT (Reactant); RACT (Reactant or reagent)  
(diribonucleotides as specific viral RNA-polymerase inhibitors for treatment or prevention of viral infections)

RN 735268-88-9 CAPLUS

CN Cytidine, N-benzoyl-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P(O)-(2-cyanoethyl)-P-doxo-2'-O-methylguanylyl-(3'→5')-N-benzoyl-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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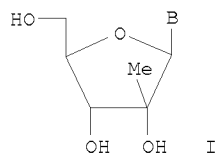
Ph

L6 ANSWER 48 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN  
 AN 2004:566635 CAPLUS  
 DN 141:89323  
 TI Process for the production of 3'-nucleoside prodrugs  
 IN Storer, Richard; Moussa, Adel; Mathieu, Steven; Qu, Lin  
 PA Idenix Cayman Limited, Cayman I.  
 SO PCT Int. Appl., 57 pp.  
 CODEN: PIXXD2

DT Patent  
 LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004058792	A1	20040715	WO 2003-US41603	20031223
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2511616	A1	20040715	CA 2003-2511616	20031223
	AU 2003300434	A1	20040722	AU 2003-300434	20031223
	US 20040181051	A1	20040916	US 2003-746395	20031223
	EP 1575971	A1	20050921	EP 2003-814400	20031223
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	BR 2003016868	A	20051025	BR 2003-16868	20031223
	CN 1751058	A	20060322	CN 2003-80109820	20031223
	JP 2006514038	T	20060427	JP 2004-562599	20031223
	NZ 540913	A	20080229	NZ 2003-540913	20031223
	ZA 2005005040	A	20060426	ZA 2005-5040	20050621
	NO 2005003557	A	20050908	NO 2005-3557	20050720
PRAI	US 2002-436150P	P	20021223		
	WO 2003-US41603	W	20031223		
OS	CASREACT 141:89323; MARPAT 141:89323				
GI					



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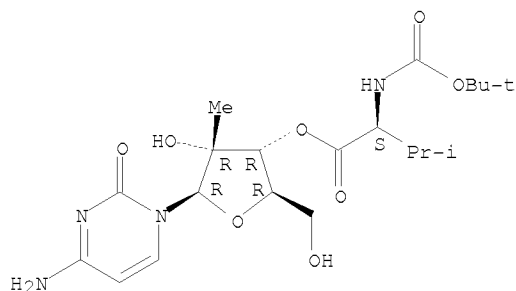
AB Provided is a single-step process for the regioselective 3'-acylation of a ribofuranosyl 2'- or 3'-branched nucleosides I, wherein B is nucleobase. These compds. are useful as antiviral agents, and in particular, can be used to treat Flaviviridae infections in a host in need thereof (no data). Thus, 9-(2'-C-methyl-3'-O-valinoyl- $\beta$ -D-ribofuranosyl)-6-N-methyladenine dihydrochloride was prepared via regioselective esterification of 9-(2'-C-methyl- $\beta$ -D-ribofuranosyl)-6-N-methyladenine with N-(tert-butoxycarbonyl)-L-valine.

IT 640725-70-8P  
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)  
(process for production of nucleoside prodrugs via regioselective esterification)

RN 640725-70-8 CAPLUS

CN L-Valine, N-[(1,1-dimethylethoxy)carbonyl]-, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry.

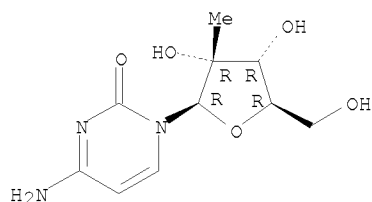


IT 20724-73-6  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(process for production of nucleoside prodrugs via regioselective esterification)

RN 20724-73-6 CAPLUS

CN Cytidine, 2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 49 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2004:453348 CAPLUS

DN 141:17578

TI Treatment of Flaviviridae infection with 2'-branched nucleosides and another mutation-inducing drug such as interferon

IN Sommadossi, Jean-Pierre; La Colla, Paolo; Standing, David; Bichko, Vadim; Qu, Lin

PA Idenix (Cayman) Limited, Cayman I.; Universita Degli Studi Di Cagliari

SO PCT Int. Appl., 166 pp.  
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004046331	A2	20040603	WO 2003-US36714	20031117
	WO 2004046331	A3	20060302		
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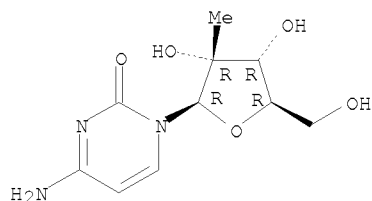
McIntosh

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

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MX 2005PA05192	A	20050908	MX 2005-PA5192	20050513
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PRAI US 2002-426675P	P	20021115		
WO 2003-US36714	W	20031117		
OS	MARPAT 141:17578			
AB	<p>The present invention discloses a method for the treatment of a Flaviviridae infection that includes the administration of a 2'-branched nucleoside, or a pharmaceutically acceptable prodrug and/or salt thereof, to a human in need of therapy in combination or alternation with a drug that directly or indirectly induces a mutation in the viral genome at a location other than a mutation of a nucleotide that results in a change from serine to a different amino acid in the highly conserved consensus sequence, XRX<u>S</u>GXXXT, of domain B of the RNA polymerase region, or is associated with such a mutation. The invention also includes a method to detect a mutant strain of Flaviviridae and a method for its treatment. Thus, in bovine viral diarrhea virus (BVDV)-infected MDBK cells treated with <math>\beta</math>-D-2'-methylcytidine, viruses resistant to the nucleoside appeared. The drug resistance was associated with a mutation in the NS5B gene which resulted in an S405T substitution in the encoded RNA-dependent RNA polymerase. These mutant viruses were sensitive to Intron A (interferon <math>\alpha</math>-2b). Intron A and <math>\beta</math>-D-2'-methylcytidine exhibited synergistic inhibitory activity on BVDV growth in MDBK cells.</p>			
IT	<p>20724-73-6</p> <p>RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)</p> <p>(treatment of Flaviviridae infection with 2'-branched nucleosides and another mutation-inducing drug such as interferon)</p>			
RN	20724-73-6 CAPLUS			
CN	Cytidine, 2'-C-methyl- (CA INDEX NAME)			

Absolute stereochemistry.



IT 640281-90-9

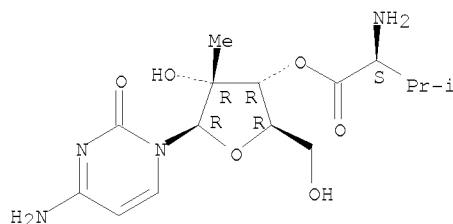
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(treatment of Flaviviridae infection with 2'-branched nucleosides and another mutation-inducing drug such as interferon)

RN 640281-90-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L6 ANSWER 50 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2004:20697 CAPLUS

DN 140:87662

TI 2'- and 3'-nucleoside prodrugs for treating Flaviviridae infections

IN Sommadossi, Jean-pierre; La Colla, Paolo; Storer, Richard; Gosselin, Gilles

PA Idenix (Cayman) Limited, Cayman I.; Centre National de la Recherche Scientifique; Universita Degli Studi di Cagliari

SO PCT Int. Appl., 2498 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 4

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US 20070060505	A1	20070315	US 2004-5472	20041206
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US 20070275883	A1	20071129	US 2006-516928	20060906

PRAI US 2002-392350P

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US 2003-470949P

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CN 2003-820501

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A3

20030627

US 2003-607909

A1

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US 2003-608907

A1

20030627

US 2003-609298

A1

20030627

WO 2003-IB3901

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20030627

WO 2004-US15395

W

20040514

OS MARPAT 140:87662

AB 2' And 3'-Prodrugs of 1'-, 2'-, 3'-, or 4'-branched  $\beta$ -D or  $\beta$ -L nucleosides, or their pharmaceutically acceptable salts and derivs., are described which are useful in the prevention and treatment of Flaviviridae infections and other related conditions. These modified nucleosides provide superior results against flaviviruses and pestiviruses, including hepatitis C virus and viruses generally that replicate through an RNA-dependent RNA reverse transcriptase. Compds., compns., methods and uses are provided for the treatment of Flaviviridae infection, including HCV infection, that include the administration of an effective amount of the prodrugs of the invention, or their pharmaceutically acceptable salts or derivs. These drugs may optionally be administered in combination or alternation with further antiviral agents to prevent or treat Flaviviridae infections and other related conditions. Preparation of compds. of the invention is included.

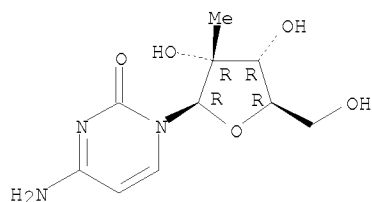
IT 20724-73-6P

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(nucleoside prodrugs for treating Flaviviridae infections)

RN 20724-73-6 CAPLUS

CN Cytidine, 2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry.



IT 125911-78-6 386213-38-3

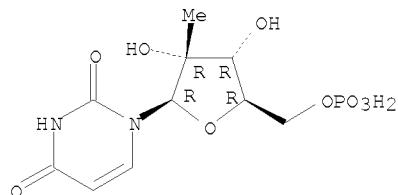
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(nucleoside prodrugs for treating Flaviviridae infections)

RN 125911-78-6 CAPLUS

CN 5'-Uridylic acid, 2'-C-methyl- (9CI) (CA INDEX NAME)

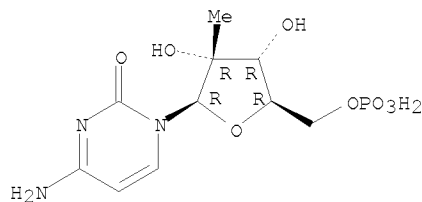
10/609,298

Absolute stereochemistry.



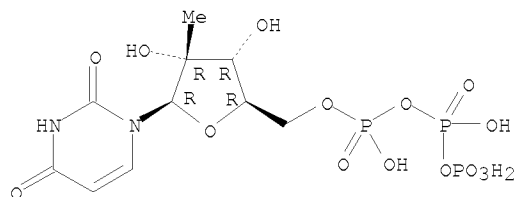
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CN 5'-Cytidylic acid, 2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



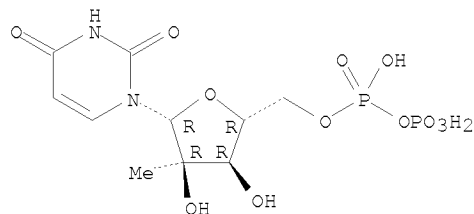
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RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);  
BIOL (Biological study)  
(nucleoside prodrugs for treating Flaviviridae infections)  
RN 125911-76-4 CAPLUS  
CN Uridine 5'-(tetrahydrogen triphosphate), 2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 150993-73-0 CAPLUS  
CN Uridine 5'-(trihydrogen diphosphate), 2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

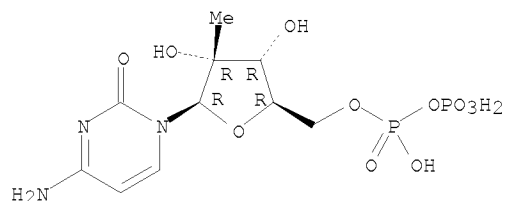


RN 640725-72-0 CAPLUS  
CN Cytidine 5'-(trihydrogen diphosphate), 2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

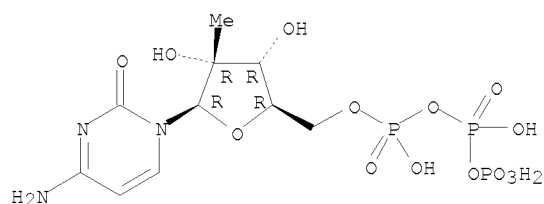
McIntosh

10/609,298



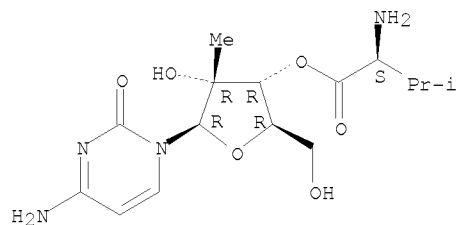
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RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);  
PKT (Pharmacokinetics); BIOL (Biological study)  
(nucleoside prodrugs for treating Flaviviridae infections)  
RN 374750-28-4 CAPLUS  
CN Cytidine 5'-(tetrahydrogen triphosphate), 2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry.



IT 640725-71-9P  
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic  
preparation); THU (Therapeutic use); BIOL (Biological study); PREP  
(Preparation); USES (Uses)  
(nucleoside prodrugs for treating Flaviviridae infections)  
RN 640725-71-9 CAPLUS  
CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA  
INDEX NAME)

Absolute stereochemistry. Rotation (+).

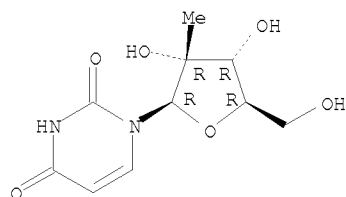


● 2 HCl

IT 31448-54-1 188413-99-2  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(nucleoside prodrugs for treating Flaviviridae infections)  
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CN Uridine, 2'-C-methyl- (CA INDEX NAME)

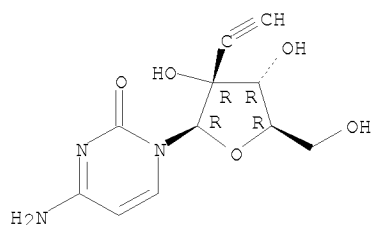
Absolute stereochemistry. Rotation (+).

10/609,298



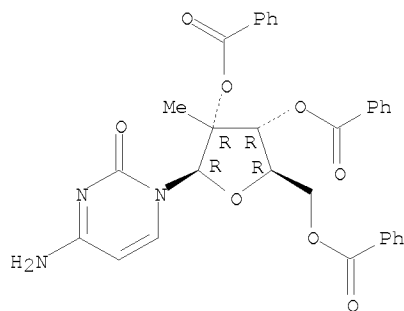
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CN Cytidine, 2'-C-ethynyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



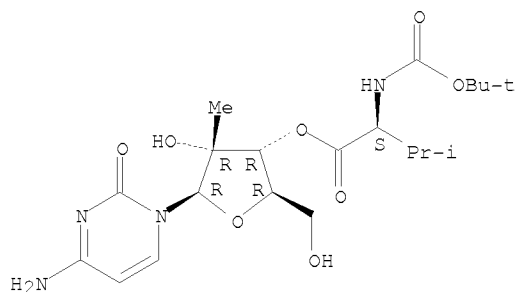
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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(nucleoside prodrugs for treating Flaviviridae infections)  
RN 640725-69-5 CAPLUS  
CN Cytidine, 2'-C-methyl-, 2',3',5'-tribenzoate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 640725-70-8 CAPLUS  
CN L-Valine, N-[(1,1-dimethylethoxy)carbonyl]-, 3'-ester with  
2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry.



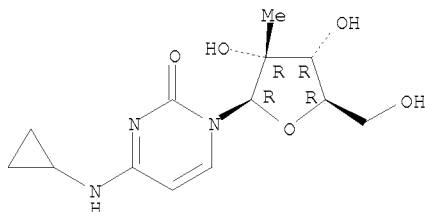
McIntosh



10/609,298

IT 622381-09-3  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(nucleoside prodrugs for treating Flaviviridae infections,  
and use with other agents)  
RN 622381-09-3 CAPLUS  
CN Cytidine, N-cyclopropyl-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

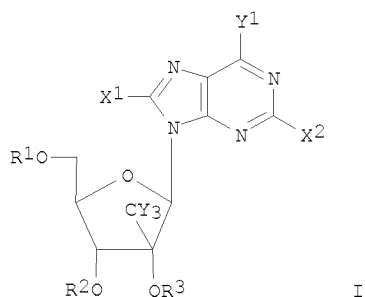


L6 ANSWER 51 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN  
AN 2004:20696 CAPLUS  
DN 140:77365  
TI Preparation of modified 2'- and 3'-nucleoside prodrugs for treating  
Flaviviridae infections  
IN Sommadossi, Jean-pierre; La Colla, Poalo; Storer, Richard; Gosselin,  
Gilles  
PA Idenix (Cayman) Limited, Cayman I.; Universita degli studi di Cagliari;  
Centre National de la Recherche Scientifique  
SO PCT Int. Appl., 201 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 4

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WO 2003-IB3246	W	20030627			
WO 2004-US15395	W	20040514			
OS MARPAT 140:77365					
GI					



AB 2' And/or 3' prodrugs of 1', 2', 3' or 4'-branched-nucleosides I, wherein R1-R3 are independently H, phosphate, alkyl, acyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, CO-aryloxyalkyl, CO-substituted aryl, sulfonate ester, benzyl, wherein the Ph group is optionally substituted with one or more substituents, alkylsulfonyl, arylsulfonyl, aralkylsulfonyl, lipid, amino acid, carbohydrate, peptide, cholesterol; Y1 is hydrogen, bromo, chloro, fluoro, iodo, CN, OH, OR4, NH2, NHR4, NR4R5, SH or SR4; X1 and X2 are independently alkyl, CH3, CF3, CY3, 2-Br-Et, CH2F, CH2Cl, CH2CF3, CF2CF3, CY2CY3, CH2OH, alkenyl, alkynyl, COOH, COOR4, COO-alkyl, COO-aryl, CO-O-alkoxyalkyl, CONH2, CONHR4, CON(R4)2, halo, CN, N3, OH, OR4, NH2, NHR4, NR4R5, SH or SR5; Y is independently H, halo; and each R4 and R5 is independently hydrogen, acyl, alkyl, lower alkyl, alkenyl, alkynyl or cycloalkyl, and their pharmaceutically acceptable salts and derivs. are described. These prodrugs are useful in the prevention and treatment of Flaviviridae infections, including HCV infection, and other related conditions. Compds. and compns. of the prodrugs of the

present invention are described. Methods and uses are also provided that include the administration of an effective amount of the prodrugs of the present invention, or their pharmaceutically acceptable salts or derivs. These drugs may optionally be administered in combination or alteration with further anti-viral agents to prevent or treat Flaviviridae infections and other related conditions. Thus, antiviral activity of  $\beta$ -D-2'-C-methyl-7-methyl-6-phenyl-3,3a,5,8a-tetrahydro-1,3,4,5,7a-penta-aza-s-indacen-8-one is reported.

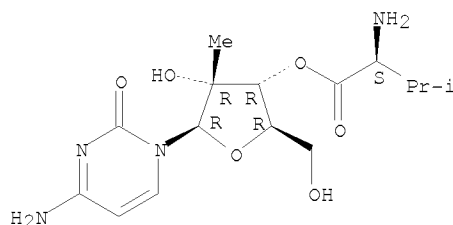
IT 640281-90-9P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of modified and nucleoside prodrugs for treating flaviviridae infections)

RN 640281-90-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



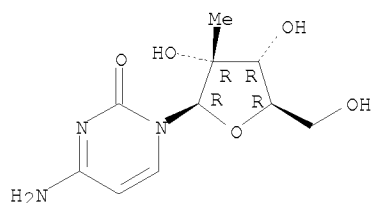
IT 20724-73-6

RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation of modified and nucleoside prodrugs for treating flaviviridae infections)

RN 20724-73-6 CAPLUS

CN Cytidine, 2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 52 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2004:20443 CAPLUS

DN 140:70984

TI 2'-C-methyl-3'-O-L-valine ester ribofuranosyl cytidine for treatment of flaviviridae infections

IN Sommadossi, Jean-Pierre; La Colla, Paolo

PA Idenix (Cayman) Limited, Cayman I.; Universita Degli Studi di Cagliari

SO PCT Int. Appl., 110 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004002422	A2	20040108	WO 2003-US20431	20030627
	WO 2004002422	A3	20050407		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				

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 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2489552 A1 20040108 CA 2003-2489552 20030627  
 AU 2003248748 A1 20040119 AU 2003-248748 20030627  
 US 20040077587 A1 20040422 US 2003-607909 20030627  
 EP 1536804 A2 20050608 EP 2003-762183 20030627

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CN 1678326 A 20051005 CN 2003-820701 20030627  
 JP 2005533824 T 20051110 JP 2004-518041 20030627  
 US 20070015905 A1 20070118 US 2003-609298 20030627  
 BR 2003012278 A 20070619 BR 2003-12278 20030627  
 NZ 537662 A 20071026 NZ 2003-537662 20030627  
 CN 101172992 A 20080507 CN 2007-10193301 20030627  
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 WO 2005020884 A2 20050310 WO 2004-US15395 20040514  
 WO 2005020884 A3 20060622

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EP 1656093 A2 20060517 EP 2004-776022 20040514  
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 US 20070032407 A1 20070208 US 2004-5473 20041206  
 US 7192936 B2 20070320  
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 NO 2005000490 A 20050127 NO 2005-490 20050127  
 US 20070275883 A1 20071129 US 2006-516928 20060906  
 IN 2007DN08806 A 20080111 IN 2007-DN8806 20071115

PRAI US 2002-392351P P 20020628  
 US 2003-466194P P 20030428  
 US 2003-470949P P 20030514  
 US 2002-392350P P 20020628  
 CN 2003-820501 A3 20030627  
 CN 2003-820701 A3 20030627  
 US 2003-607909 A1 20030627  
 US 2003-608907 A1 20030627  
 US 2003-609298 A1 20030627  
 WO 2003-US20431 W 20030627  
 WO 2004-US15395 W 20040514  
 IN 2005-DN344 A3 20050128

OS MARPAT 140:70984

AB The 3'-L-valine ester of  $\beta$ -D-2'-C-methyl-ribofuranosyl cytidine  
 provides superior results against flaviviruses and  
 pestiviruses, including hepatitis C virus.  
 Based on this discovery, compds., compns., methods and uses are provided  
 for the treatment of flaviviridae, including HCV, that  
 include the administration of an effective amount of val-mCyd or its salt,

ester, prodrug or derivative, optionally in a pharmaceutically acceptable carrier. In an alternative embodiment, val-mCyd is used to treat any virus that replicates through an RNA-dependent RNA polymerase. Several examples are provided of the pharmacol., mechanism of action, metabolism, side effects, and clin. efficacy of the title compound

IT 640281-90-9D, salts 642075-50-1 642075-51-2

642075-52-3 642075-53-4 642075-54-5

642075-55-6 642075-56-7 642075-57-8

642075-58-9 642075-59-0 642075-60-3

642075-61-4 642075-62-5 642075-63-6

642075-64-7 642075-65-8 642075-66-9

642075-67-0 642075-68-1 642075-69-2

642075-70-5 642075-71-6 642075-72-7

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642075-77-2

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

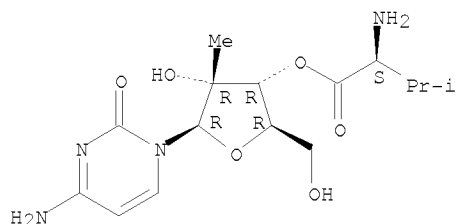
(ribofuranosylcytidine methylvaline ester combined with other

antivirals for treatment of flaviviridae infections)

RN 640281-90-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 642075-50-1 CAPLUS

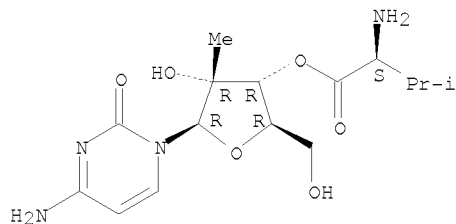
CN L-Valine, 3'-ester with 2'-C-methylcytidine, 4-methylbenzenesulfonate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

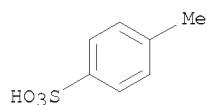
Absolute stereochemistry. Rotation (+).



CM 2

CRN 104-15-4

CMF C7 H8 O3 S



RN 642075-51-2 CAPLUS

McIntosh

10/609,298

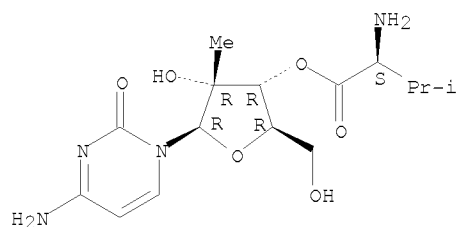
CN L-Valine, 3'-ester with 2'-C-methylcytidine, methanesulfonate (salt) (9CI)  
(CA INDEX NAME)

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

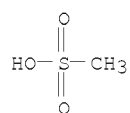
Absolute stereochemistry. Rotation (+).



CM 2

CRN 75-75-2

CMF C H4 O3 S



RN 642075-52-3 CAPLUS

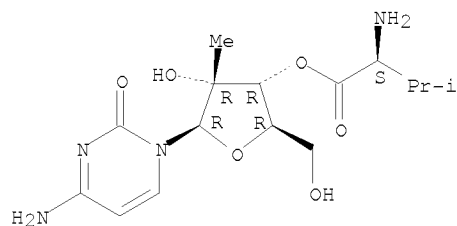
CN L-Valine, 3'-ester with 2'-C-methylcytidine, acetate (salt) (9CI) (CA  
INDEX NAME)

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

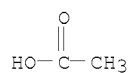
Absolute stereochemistry. Rotation (+).



CM 2

CRN 64-19-7

CMF C2 H4 O2



RN 642075-53-4 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2-hydroxy-1,2,3-

McIntosh

10/609,298

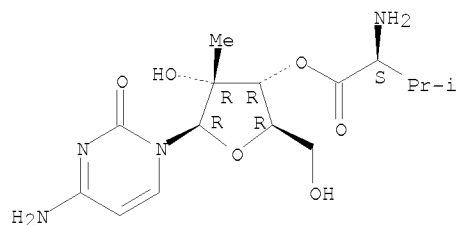
propanetricarboxylate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

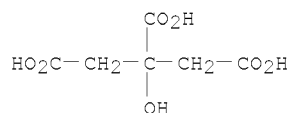
Absolute stereochemistry. Rotation (+).



CM 2

CRN 77-92-9

CMF C6 H8 O7



RN 642075-54-5 CAPLUS

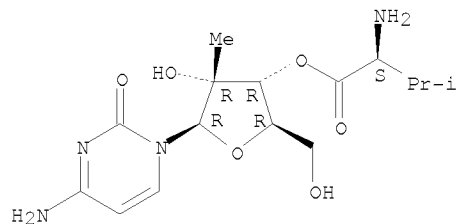
CN L-Valine, 3'-ester with 2'-C-methylcytidine, propanedioate (salt) (9CI)  
(CA INDEX NAME)

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

CRN 141-82-2

CMF C3 H4 O4

HO2C-CH2-CO2H

RN 642075-55-6 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, (2R,3R)-2,3-dihydroxybutanedioate (salt) (9CI) (CA INDEX NAME)

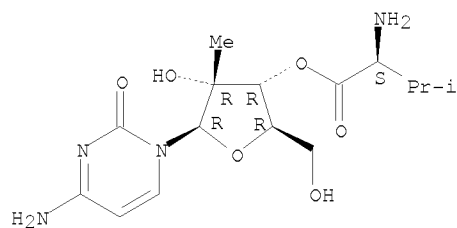
CM 1

McIntosh

10/609,298

CRN 640281-90-9  
CMF C15 H24 N4 O6

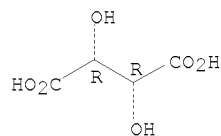
Absolute stereochemistry. Rotation (+).



CM 2

CRN 87-69-4  
CMF C4 H6 O6

Absolute stereochemistry.

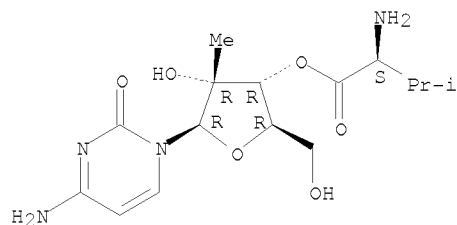


RN 642075-56-7 CAPLUS  
CN L-Valine, 3'-ester with 2'-C-methylcytidine, butanedioate (salt) (9CI)  
(CA INDEX NAME)

CM 1

CRN 640281-90-9  
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

CRN 110-15-6  
CMF C4 H6 O4

HO<sub>2</sub>C-CH<sub>2</sub>-CH<sub>2</sub>-CO<sub>2</sub>H

RN 642075-57-8 CAPLUS  
CN L-Valine, 3'-ester with 2'-C-methylcytidine, benzoate (salt) (9CI) (CA  
INDEX NAME)

CM 1

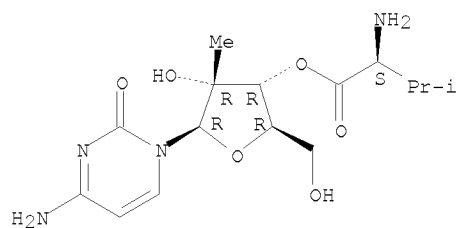
McIntosh



10/609,298

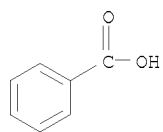
CRN 640281-90-9  
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

CRN 65-85-0  
CMF C7 H6 O2

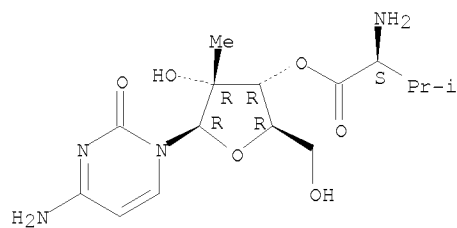


RN 642075-58-9 CAPLUS  
CN L-Ascorbic acid, compd. with L-valine 3'-ester with 2'-C-methylcytidine  
(9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9  
CMF C15 H24 N4 O6

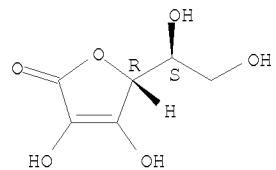
Absolute stereochemistry. Rotation (+).



CM 2

CRN 50-81-7  
CMF C6 H8 O6

Absolute stereochemistry.



RN 642075-59-0 CAPLUS

McIntosh

10/609,298

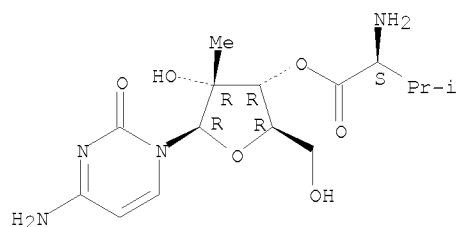
CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2-oxopentanedioate (salt)  
(9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

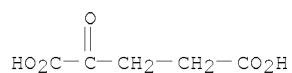
Absolute stereochemistry. Rotation (+).



CM 2

CRN 328-50-7

CMF C5 H6 O5



RN 642075-60-3 CAPLUS

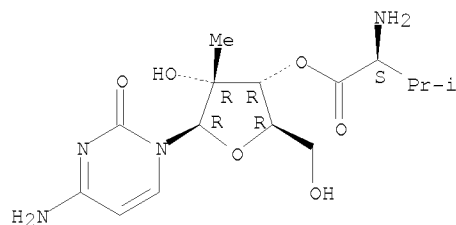
CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2,3-dihydroxypropyl phosphate  
(salt) (9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

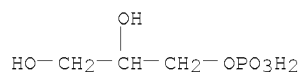
Absolute stereochemistry. Rotation (+).



CM 2

CRN 57-03-4

CMF C3 H9 O6 P



RN 642075-61-4 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, formate (salt) (9CI) (CA  
INDEX NAME)

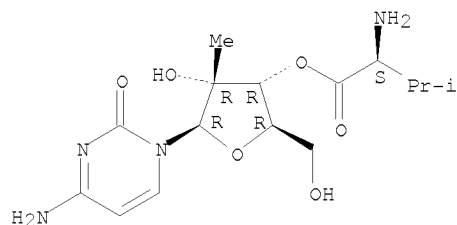
McIntosh

10/609,298

CM 1

CRN 640281-90-9  
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

CRN 64-18-6  
CMF C H2 O2

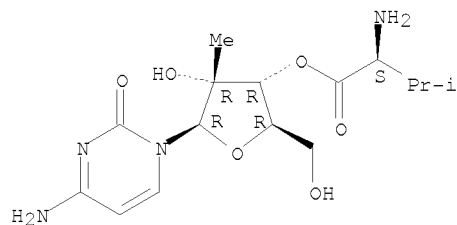
O=CH-OH

RN 642075-62-5 CAPLUS  
CN L-Valine, 3'-ester with 2'-C-methylcytidine, (2E)-2-butenedioate (salt)  
(9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9  
CMF C15 H24 N4 O6

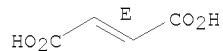
Absolute stereochemistry. Rotation (+).



CM 2

CRN 110-17-8  
CMF C4 H4 O4

Double bond geometry as shown.



RN 642075-63-6 CAPLUS  
CN L-Valine, 3'-ester with 2'-C-methylcytidine, propanoate (salt) (9CI) (CA  
INDEX NAME)

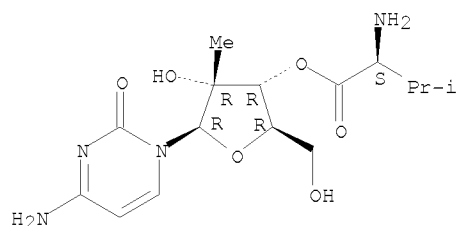
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CMF C15 H24 N4 O6

McIntosh

10/609,298

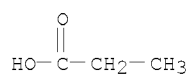
Absolute stereochemistry. Rotation (+).



CM 2

CRN 79-09-4

CMF C3 H6 O2



RN 642075-64-7 CAPLUS

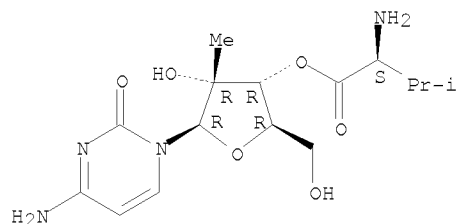
CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydroxyacetate (salt) (9CI)  
(CA INDEX NAME)

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

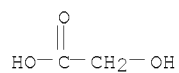
Absolute stereochemistry. Rotation (+).



CM 2

CRN 79-14-1

CMF C2 H4 O3



RN 642075-65-8 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2-hydroxypropanoate (salt)  
(9CI) (CA INDEX NAME)

CM 1

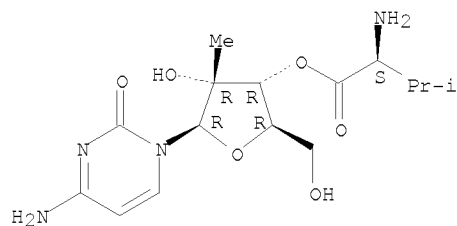
CRN 640281-90-9

CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).

McIntosh

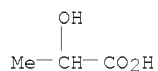
10/609,298



CM 2

CRN 50-21-5

CMF C3 H6 O3



RN 642075-66-9 CAPLUS

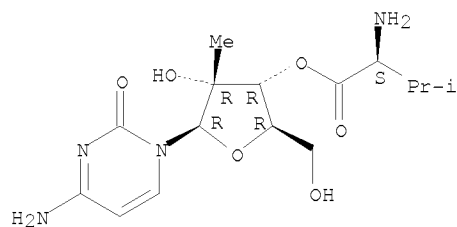
CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2-oxopropanoate (salt) (9CI)  
(CA INDEX NAME)

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

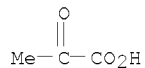
Absolute stereochemistry. Rotation (+).



CM 2

CRN 127-17-3

CMF C3 H4 O3



RN 642075-67-0 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, ethanedioate (salt) (9CI)  
(CA INDEX NAME)

CM 1

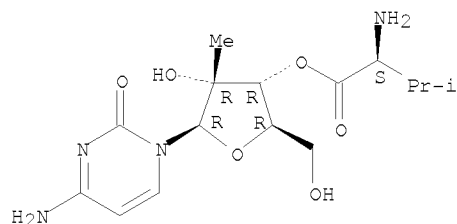
CRN 640281-90-9

CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).

McIntosh

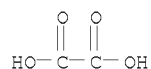
10/609,298



CM 2

CRN 144-62-7

CMF C2 H2 O4



RN 642075-68-1 CAPLUS

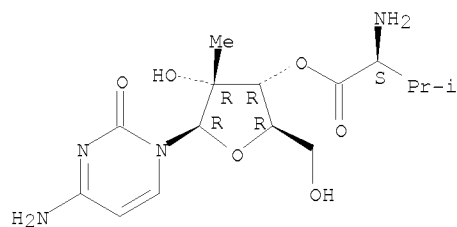
CN L-Valine, 3'-ester with 2'-C-methylcytidine, (2Z)-2-butenedioate (salt)  
(9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).

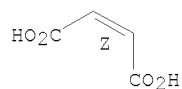


CM 2

CRN 110-16-7

CMF C4 H4 O4

Double bond geometry as shown.



RN 642075-69-2 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2-hydroxybenzoate (salt)  
(9CI) (CA INDEX NAME)

CM 1

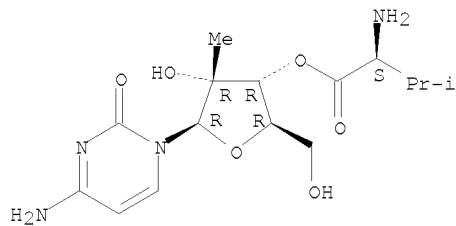
CRN 640281-90-9

CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).

McIntosh

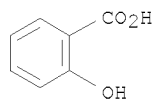
10/609,298



CM 2

CRN 69-72-7

CMF C7 H6 O3



RN 642075-70-5 CAPLUS

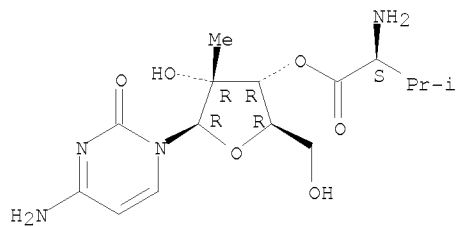
CN	L-Valine, 3'-ester with 2'-C-methylcytidine, sulfate (salt) (9CI) (CA INDEX NAME)
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CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

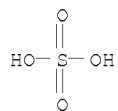
Absolute stereochemistry. Rotation (+).



CM 2

CRN 7664-93-9

CMF H2 O4 S



RN 642075-71-6 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, nitrate (salt) (9CI) (CA  
INDEX NAME)

CM 1

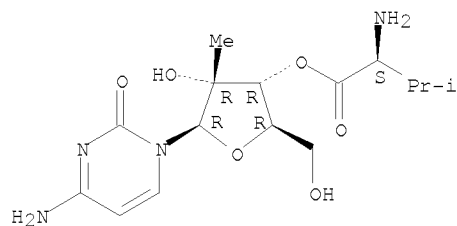
CRN 640281-90-9

CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).

McIntosh

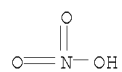
10/609,298



CM 2

CRN 7697-37-2

CMF H N O3



RN 642075-72-7 CAPLUS

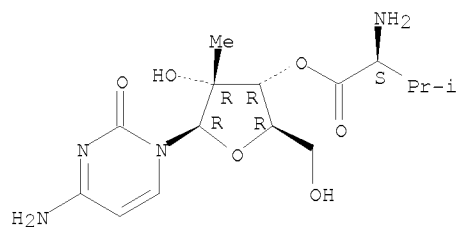
CN L-Valine, 3'-ester with 2'-C-methylcytidine, carbonate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

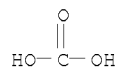
Absolute stereochemistry. Rotation (+).



CM 2

CRN 463-79-6

CMF C H2 O3



RN 642075-74-9 CAPLUS

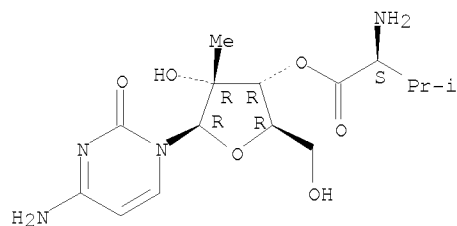
CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrobromide (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

McIntosh



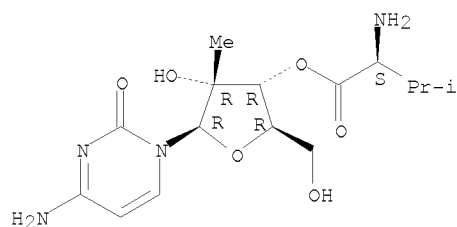
10/609,298



● x HBr

RN 642075-75-0 CAPLUS  
CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydriodide (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



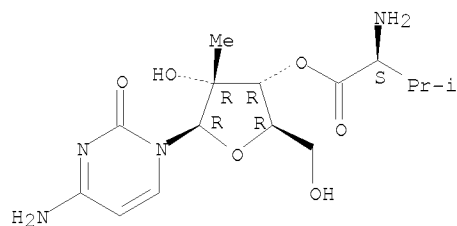
● x HI

RN 642075-76-1 CAPLUS  
CN L-Valine, 3'-ester with 2'-C-methylcytidine, carbonate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

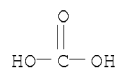
CRN 640281-90-9  
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

CRN 463-79-6  
CMF C H2 O3



McIntosh

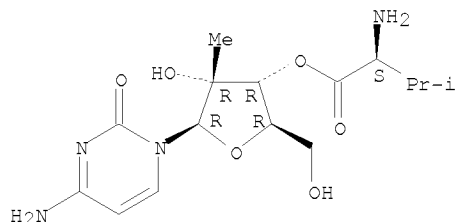
10/609,298

RN 642075-77-2 CAPLUS  
CN L-Valine, 3'-ester with 2'-C-methylcytidine, phosphate (salt) (9CI) (CA INDEX NAME)

CM 1

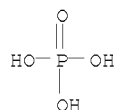
CRN 640281-90-9  
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



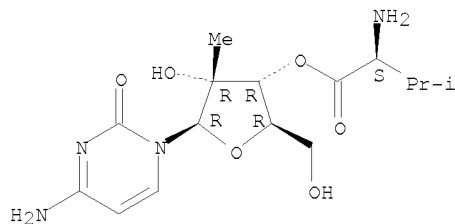
CM 2

CRN 7664-38-2  
CMF H3 O4 P



IT 640281-90-9P  
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(ribofuranosylcytidine methylvaline ester for treatment of flaviviridae infections)  
RN 640281-90-9 CAPLUS  
CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

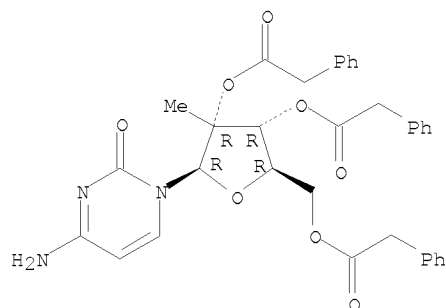


IT 642075-41-0  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(ribofuranosylcytidine methylvaline ester for treatment of flaviviridae infections)  
RN 642075-41-0 CAPLUS  
CN Cytidine, 2'-C-methyl-, 2',3',5'-tris(benzeneacetate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

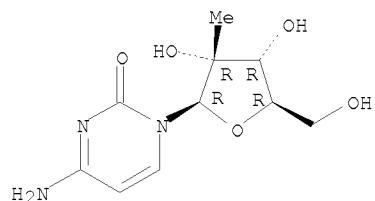
McIntosh

10/609,298



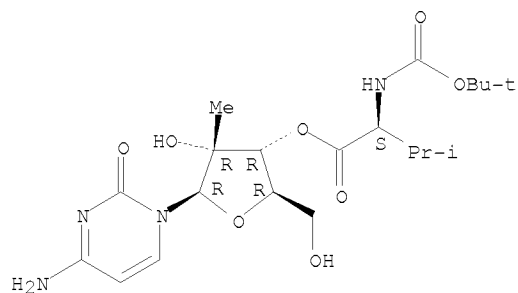
IT 20724-73-6P 640725-70-8P 642075-42-1P  
642075-43-2P 642075-44-3P 642075-48-7P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(ribofuranosylcytidine methylvaline ester for treatment of  
flaviviridae infections)  
RN 20724-73-6 CAPLUS  
CN Cytidine, 2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry.



RN 640725-70-8 CAPLUS  
CN L-Valine, N-[(1,1-dimethylethoxy)carbonyl]-, 3'-ester with  
2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry.

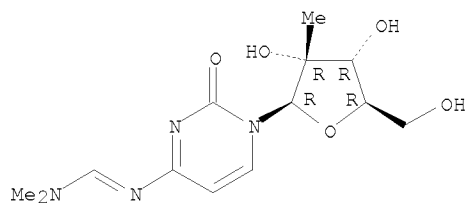


RN 642075-42-1 CAPLUS  
CN Cytidine, N-[(dimethylamino)methylene]-2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry unknown.

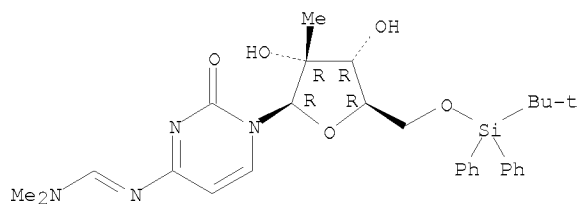
McIntosh

10/609,298



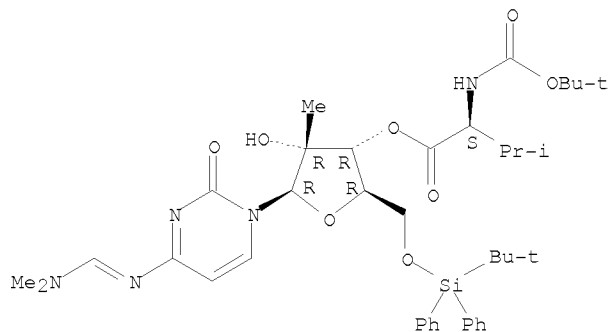
RN 642075-43-2 CAPLUS  
CN Cytidine, N-[(dimethylamino)methylene]-5'-O-[(1,1-dimethylethyl)diphenylsilyl]-2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry unknown.



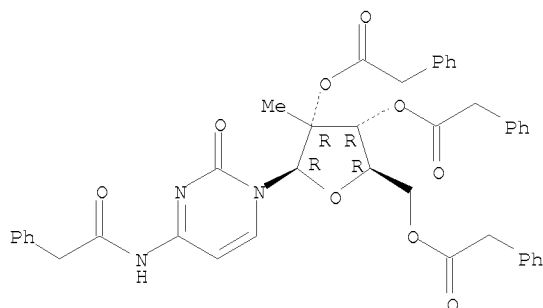
RN 642075-44-3 CAPLUS  
CN L-Valine, N-[(1,1-dimethylethoxy)carbonyl]-, 3'-ester with 5'-O-[(1,1-dimethylethyl)diphenylsilyl]-N-[(dimethylamino)methylene]-2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry unknown.



RN 642075-48-7 CAPLUS  
CN Cytidine, 2'-C-methyl-N-(phenylacetyl)-, 2',3',5'-tris(benzeneacetate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

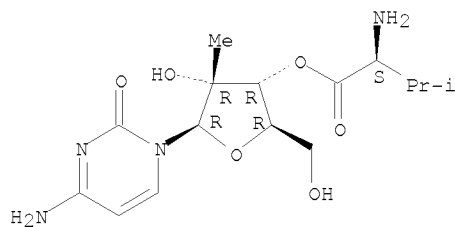


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IT  640725-71-9P
    RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
    study); PREP (Preparation); USES (Uses)
        (ribofuranosylcytidine methylvaline ester for treatment of
        flaviviridae infections)
RN  640725-71-9  CAPLUS
CN  L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2)  (CA
    INDEX NAME)

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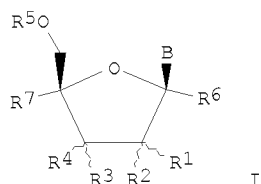
Absolute stereochemistry. Rotation (+).

 $\bullet 2 \text{ HCl}$ 

L6 ANSWER 53 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN  
AN 2004:2898 CAPLUS  
DN 140:42424  
TI Preparation of nucleoside derivatives as inhibitors of RNA-dependent RNA  
viral polymerase  
IN Carroll, Steven S.; Olsen, David B.; Durette, Philippe L.; Bhat,  
Balkrishen; Dande, Prasad; Eldrup, Anne B.  
PA Merck & Co., Inc., USA; Isis Pharmaceuticals, Inc.  
SO PCT Int. Appl., 43 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004000858	A2	20031231	WO 2003-US19172	20030617
	WO 2004000858	A3	20050512		
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	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	CA 2488534	A1	20031231	CA 2003-2488534	20030617
	AU 2003269890	A1	20040106	AU 2003-269890	20030617

EP 1551421                    A2        20050713        EP 2003-751777                    20030617  
           R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
                                  IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK  
 JP 2005530843                    T        20051013                    JP 2004-515870                    20030617  
 US 20070004669                    A1        20070104                    US 2006-517295                    20060615  
 PRAI US 2002-390579P                    P        20020621  
 WO 2003-US19172                    W        20030617  
 OS        MARPAT 140:42424  
 GI



AB    The present invention provides nucleoside compds. I, wherein B is nucleobase; R1 is fluoromethyl, difluoromethyl, trifluoromethyl; R2 is H, F, amino, OH, SH, alkoxy, alkylcarbonyloxy, alkyl; R3 and R4 are independently H, Cn, N3, halogen, OH, SH, amino, alkoxy, alkylcarbonyloxy, alkenyl, alkynyl; R5 is H, alkylcarbonyl, P3O9H4, P2O6H3, phosphophonyl; R6 and R7 independently H, Me, hydroxymethyl, fluoromethyl; and certain derivs. thereof which are inhibitors of RNA-dependent RNA viral polymerase. These compds. are inhibitors of RNA-dependent RNA viral replication and are useful for the treatment of RNA-dependent RNA viral infection. They are particularly useful as inhibitors of hepatitis C virus (HCV) NS5B polymerase, as inhibitors of HCV replication, and/or for the treatment of hepatitis C infection. The invention also describes pharmaceutical compns. containing such nucleoside compds. alone or in combination with other agents active against RNA-dependent RNA viral infection, in particular HCV infection. Also disclosed are methods of inhibiting RNA-dependent RNA polymerase, inhibiting RNA-dependent RNA viral replication, and/or treating RNA-dependent RNA viral infection with the nucleoside compds. of the present invention. Thus, 2-amino-9-(2-C-fluoromethyl-β-D-ribofuranosyl)-3,9-dihydropurin-6-one was prepared and tested as inhibitor of RNA-dependent RNA viral polymerase. Title compds. tested in the HCV NS5B polymerase assay exhibited IC50's less than 100 μmol.

IT    510765-51-2P 636581-91-4P 636581-92-5P  
       636581-93-6P 636582-01-9P 636582-02-0P  
       636582-03-1P 636582-04-2P

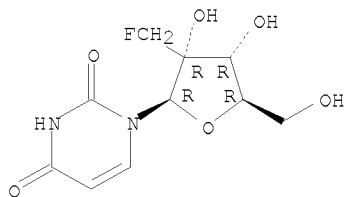
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of nucleoside derivs. as inhibitors of RNA-dependent RNA viral polymerase)

RN    510765-51-2    CAPLUS

CN    Uridine, 2'-C-(fluoromethyl)-    (CA INDEX NAME)

Absolute stereochemistry.

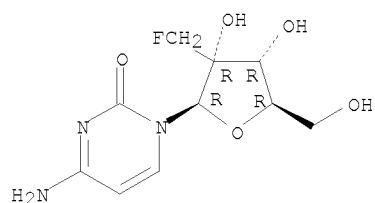


RN    636581-91-4    CAPLUS

CN    Cytidine, 2'-C-(fluoromethyl)- (9CI)    (CA INDEX NAME)

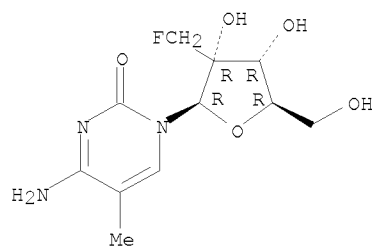
10/609,298

Absolute stereochemistry.



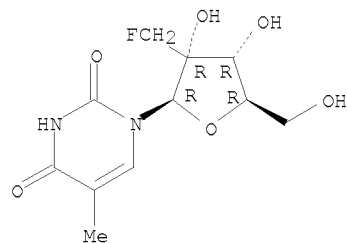
RN 636581-92-5 CAPLUS  
CN Cytidine, 2'-C-(fluoromethyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



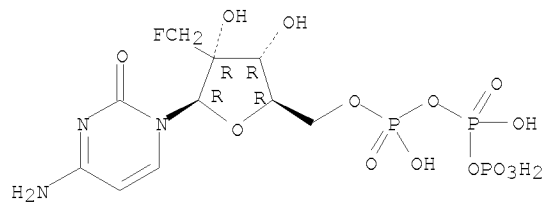
RN 636581-93-6 CAPLUS  
CN Uridine, 2'-C-(fluoromethyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 636582-01-9 CAPLUS  
CN Cytidine 5'-(tetrahydrogen triphosphate), 2'-C-(fluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

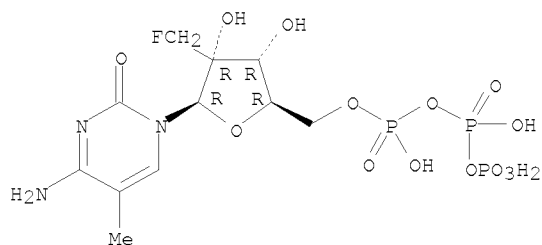


RN 636582-02-0 CAPLUS  
CN Cytidine 5'-(tetrahydrogen triphosphate), 2'-C-(fluoromethyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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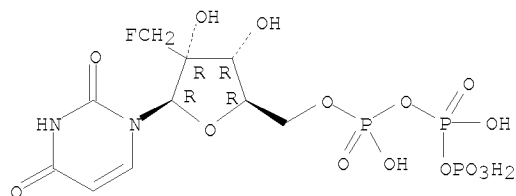
10/609,298



RN 636582-03-1 CAPLUS

CN Uridine 5'-(tetrahydrogen triphosphate), 2'-C-(fluoromethyl)- (9CI) (CA INDEX NAME)

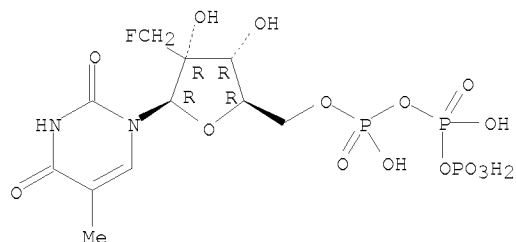
Absolute stereochemistry.



RN 636582-04-2 CAPLUS

CN Uridine 5'-(tetrahydrogen triphosphate), 2'-C-(fluoromethyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 54 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2003:892793 CAPLUS

DN 139:365176

TI Preparation of nucleoside derivatives for treating hepatitis C virus infection

IN Roberts, Christopher Don; Dyatkina, Natalia B.; Keicher, Jesse D.; Liehr, Sebastian Johannes Reinhard; Hanson, Eric Jason

PA Genelabs Technologies, Inc., USA

SO PCT Int. Appl., 182 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

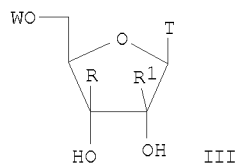
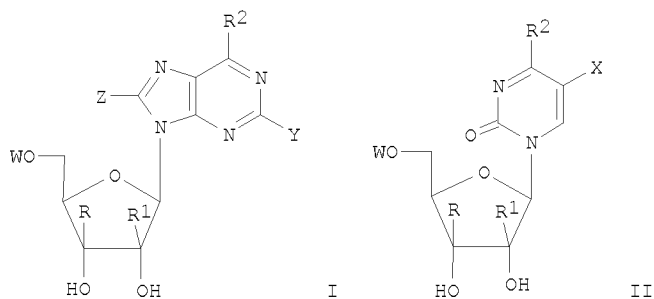
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003093290	A2	20031113	WO 2003-US14237	20030506
	WO 2003093290	A3	20040318		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				

McIntosh



RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2484921	A1	20031113	CA 2003-2484921	20030506
AU 2003232071	A1	20031117	AU 2003-232071	20030506
US 20040063658	A1	20040401	US 2003-431631	20030506
EP 1501850	A2	20050202	EP 2003-747674	20030506
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BR 2003009581	A	20050329	BR 2003-9581	20030506
CN 1653077	A	20050810	CN 2003-810239	20030506
JP 2005530759	T	20051013	JP 2004-501429	20030506
NZ 536123	A	20060929	NZ 2003-536123	20030506
MX 2004PA10983	A	20050214	MX 2004-PA10983	20041105
NO 2004005247	A	20041130	NO 2004-5247	20041130
PRAI US 2002-378624P	P	20020506		
US 2002-392871P	P	20020628		
WO 2003-US14237	W	20030506		
OS MARPAT 139:365176				
GI				



AB Nucleosides I-III, wherein R and R1 are independently H, alkyl, alkenyl, alkynyl, provided that R and R1 are not both H; R2 is alkyl, cycloalkyl, alkenyl, alkynyl, acylamino, guanidino, amidino, thioacylamino, OH, alkoxy, halo, nitro, aryl, heteroaryl, substituted amine; W is H, phosphate, phosphonate, acyl, alkyl, sulfonate, lipid, amino acid, sugar residue, peptide, cholesterol; X is H, halo, alkyl, substituted amine; Y is H, halo, OH, alkylthio, substituted amine; Z is H, halo, OH, alkyl, substituted amine; T is nucleobase, were prepared as HCV RNA polymerase inhibitors and for treating hepatitis C virus infections. Thus, 2-(4-amino-pyrrolo[3,2-c]pyridin-1-yl)-5-hydroxymethyl-3-methyltetrahydro-furan-3,4-diol was prepared for treating hepatitis C virus infections (no data). Different kind of formulation such as tablet, capsule, suspension, injectable, and suppository formulation are reported.

IT 31448-54-1P 119410-84-3P 622380-51-2P  
 622380-52-3P 622380-56-7P 622380-57-8P  
 622380-59-0P 622380-60-3P 622380-61-4P  
 622380-89-6P 622380-90-9P 622381-09-3P  
 622381-10-6P  
 RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

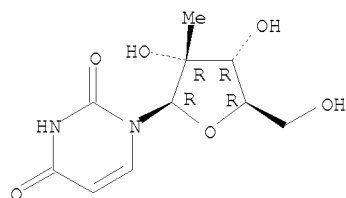
10/609,298

(preparation of nucleoside derivs. for treating hepatitis  
C virus infection)

RN 31448-54-1 CAPLUS

CN Uridine, 2'-C-methyl- (CA INDEX NAME)

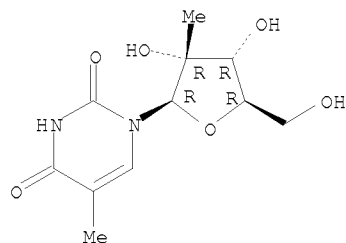
Absolute stereochemistry. Rotation (+).



RN 119410-84-3 CAPLUS

CN Uridine, 5-methyl-2'-C-methyl- (9CI) (CA INDEX NAME)

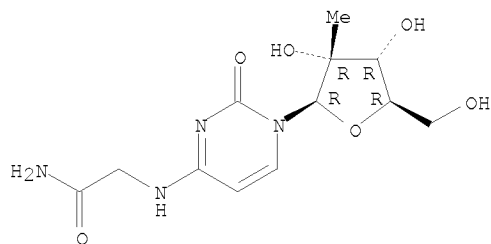
Absolute stereochemistry. Rotation (+).



RN 622380-51-2 CAPLUS

CN Cytidine, N-(2-amino-2-oxoethyl)-2'-C-methyl- (9CI) (CA INDEX NAME)

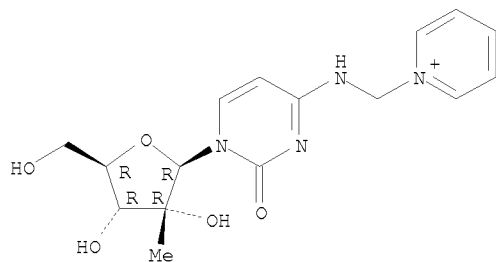
Absolute stereochemistry.



RN 622380-52-3 CAPLUS

CN Pyridinium, 1-[[[1,2-dihydro-1-(2-C-methyl-β-D-ribofuranosyl)-2-oxo-4-pyrimidinyl]amino]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



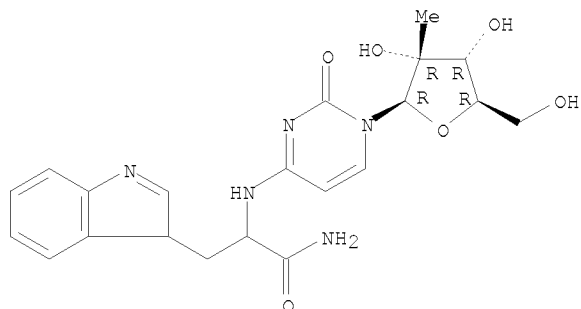
McIntosh

10/609,298

RN 622380-56-7 CAPLUS

CN Cytidine, N-[2-amino-1-(3H-indol-3-ylmethyl)-2-oxoethyl]-2'-C-methyl-  
(9CI) (CA INDEX NAME)

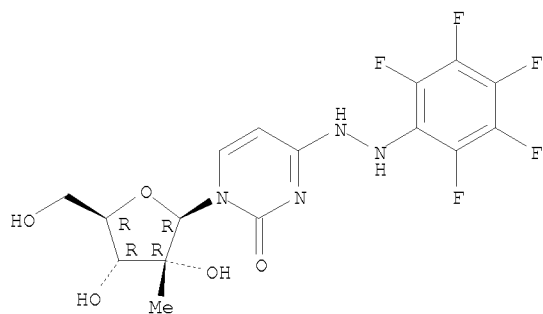
Absolute stereochemistry.



RN 622380-57-8 CAPLUS

CN Uridine, 2'-C-methyl-, 4-[(pentafluorophenyl)hydrazone] (9CI) (CA INDEX  
NAME)

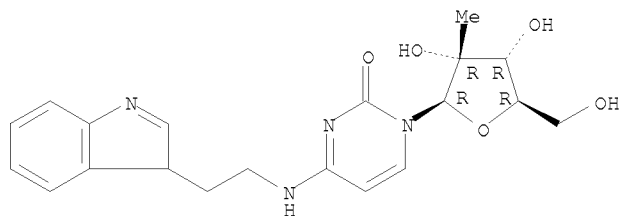
Absolute stereochemistry.



RN 622380-59-0 CAPLUS

CN Cytidine, N-[2-(3H-indol-3-yl)ethyl]-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

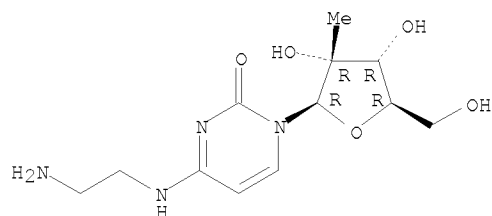


RN 622380-60-3 CAPLUS

CN Cytidine, N-(2-aminoethyl)-2'-C-methyl- (9CI) (CA INDEX NAME)

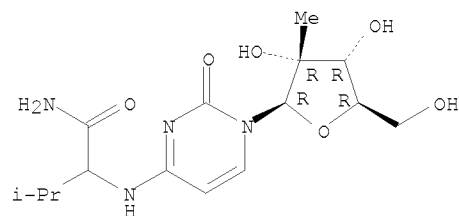
Absolute stereochemistry.

10/609,298



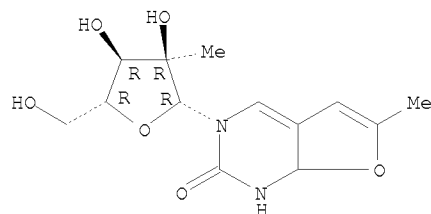
RN 622380-61-4 CAPLUS  
CN Cytidine, N-[1-(aminocarbonyl)-2-methylpropyl]-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



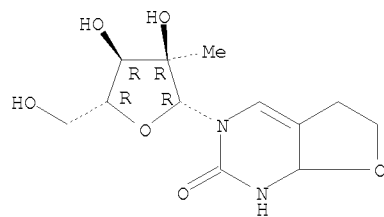
RN 622380-89-6 CAPLUS  
CN Furo[2,3-d]pyrimidin-2(1H)-one, 3,7a-dihydro-6-methyl-3-(2-C-methyl-β-D-ribofuranosyl)- (CA INDEX NAME)

Absolute stereochemistry.



RN 622380-90-9 CAPLUS  
CN Furo[2,3-d]pyrimidin-2(1H)-one, 3,5,6,7a-tetrahydro-3-(2-C-methyl-β-D-ribofuranosyl)- (CA INDEX NAME)

Absolute stereochemistry.

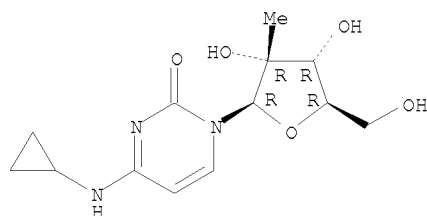


RN 622381-09-3 CAPLUS  
CN Cytidine, N-cyclopropyl-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

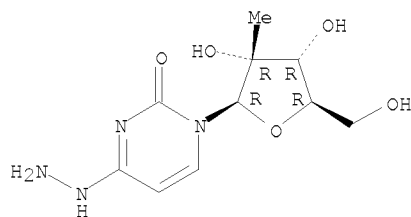
McIntosh

10/609,298



RN 622381-10-6 CAPLUS  
CN Uridine, 2'-C-methyl-, 4-hydrazone (9CI) (CA INDEX NAME)

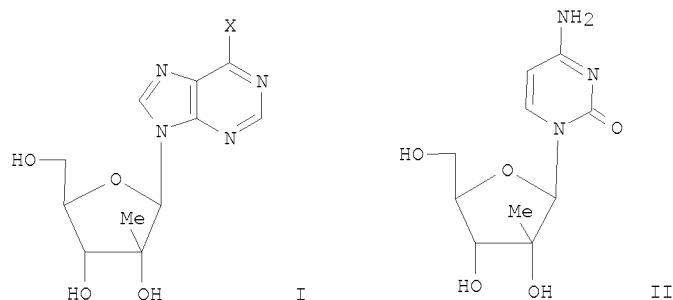
Absolute stereochemistry.



L6 ANSWER 55 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN  
AN 2003:591195 CAPLUS  
DN 139:133789  
TI Preparation of sugar modified nucleosides as antiviral agents  
IN Hong, Zhi; An, Haoyun; Ding, Yili; Girardet, Jean-luc; Zhong, Weidong  
PA Ribapharm Inc., USA  
SO PCT Int. Appl., 33 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003062255	A2	20030731	WO 2002-US231556	20021002
	WO 2003062255	A3	20060908		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	EP 1572705	A2	20050914	EP 2002-776103	20021002
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK			
	US 20070032448	A1	20070208	US 2006-535742	20060925
PRAI	US 2002-350296P	P	20020117		
	US 2002-391800P	P	20020626		
	WO 2002-US31556	W	20021002		
OS	MARPAT 139:133789				
GI					

McIntosh



AB Various 2'-modified nucleoside analogs I and II wherein X is NH<sub>2</sub>, NHMe, NMe<sub>2</sub>, OMe, SMe, and corresponding prodrugs are provided, and particularly contemplated methods of use include use as antiviral agents, and especially as antiviral agents against HCV.

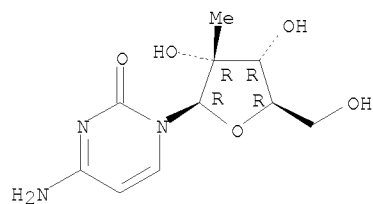
IT 20724-73-6 31448-54-1 119410-84-3  
565451-07-2 565451-08-3 565451-09-4  
565451-10-7 565451-11-8

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(preparation of sugar modified nucleosides as antiviral agents)

RN 20724-73-6 CAPLUS

CN Cytidine, 2'-C-methyl- (CA INDEX NAME)

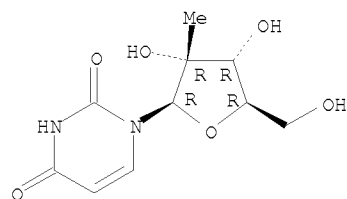
Absolute stereochemistry.



RN 31448-54-1 CAPLUS

CN Uridine, 2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

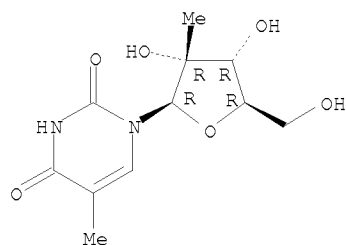


RN 119410-84-3 CAPLUS

CN Uridine, 5-methyl-2'-C-methyl- (9CI) (CA INDEX NAME)

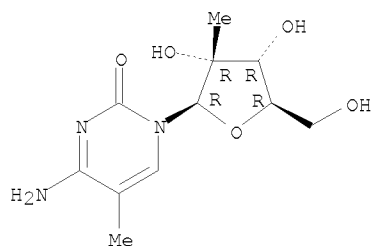
Absolute stereochemistry. Rotation (+).

10/609,298



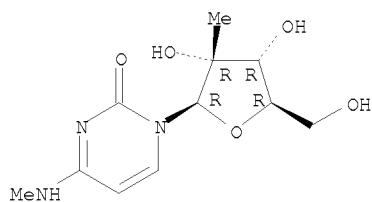
RN 565451-07-2 CAPLUS  
CN Cytidine, 5-methyl-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



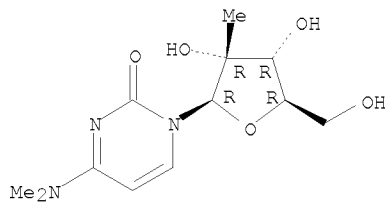
RN 565451-08-3 CAPLUS  
CN Cytidine, N-methyl-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 565451-09-4 CAPLUS  
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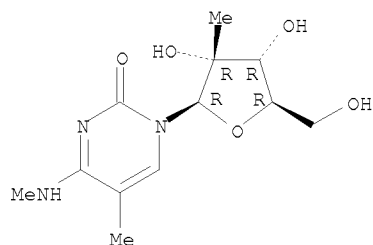
Absolute stereochemistry.



RN 565451-10-7 CAPLUS  
CN Cytidine, N,5-dimethyl-2'-C-methyl- (9CI) (CA INDEX NAME)

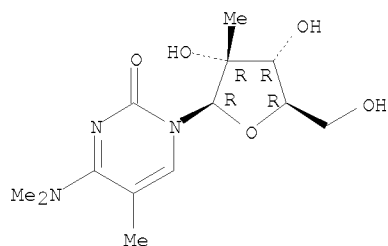
Absolute stereochemistry.

McIntosh



RN 565451-11-8 CAPLUS  
 CN Cytidine, N,N,5-trimethyl-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

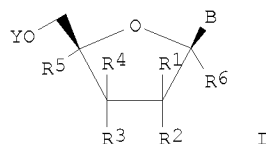


L6 ANSWER 56 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN  
 AN 2002:555629 CAPLUS  
 DN 137:125359  
 TI Preparation of nucleoside derivatives as inhibitors of RNA-dependent RNA  
 viral polymerase  
 IN Carroll, Steven S.; Lafemina, Robert L.; Hall, Dawn L.; Himmelberger, Amy  
 L.; Kuo, Lawrence C.; Maccoss, Malcolm; Olsen, David B.; Rutkowski, Carrie  
 A.; Tomassini, Joanne E.; An, Haoyun; Bhat, Balkrishen; Bhat, Neelima;  
 Cook, Phillip Dan; Eldrup, Anne B.; Guinosso, Charles J.; Prhavo, Marija;  
 Prakash, Thazha P.  
 PA Merck & Co., Inc., USA; Isis Pharmaceuticals, Inc.  
 SO PCT Int. Appl., 235 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002057425	A2	20020725	WO 2002-US1531	20020118
WO 2002057425	A3	20050421		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2433878	A1	20020725	CA 2002-2433878	20020118
AU 2002243600	A1	20020730	AU 2002-243600	20020118
AU 2002243600	B2	20060928		
US 20020147160	A1	20021010	US 2002-52318	20020118
US 6777395	B2	20040817		
CN 1498221	A	20040519	CN 2002-806977	20020118
JP 2004532184	T	20041021	JP 2002-558479	20020118
EP 1539188	A2	20050615	EP 2002-709095	20020118
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EP 1707571	A1	20061004	EP 2006-76021	20020118
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,			



IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
	ES 2278009	T3	20070801	ES 2002-709299	20020118
	TW 261056	B	20060901	TW 2002-91100893	20020121
	US 20040072788	A1	20040415	US 2003-431657	20030507
	ZA 2003005078	A	20040521	ZA 2003-5078	20030630
	US 20040067901	A1	20040408	US 2003-688691	20031017
	US 7125855	B2	20061024		
	US 20040110717	A1	20040610	US 2004-250873	20040116
	US 7105499	B2	20060912		
	US 20050272676	A1	20051208	US 2005-200499	20050809
	US 20060205686	A1	20060914	US 2005-236224	20050927
	US 20060264390	A1	20061123	US 2006-496338	20060731
	US 7202224	B2	20070410		
	US 20070275912	A1	20071129	US 2006-643464	20061221
	JP 2007224045	A	20070906	JP 2007-115345	20070425
PRAI	US 2001-263313P	P	20010122		
	US 2001-282069P	P	20010406		
	US 2001-299320P	P	20010619		
	US 2001-344528P	P	20011025		
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	JP 2002-558479	A3	20020118		
	US 2002-52318	A3	20020118		
	WO 2002-US1531	W	20020118		
	US 2003-431657	B1	20030507		
	US 2003-688691	A1	20031017		
	US 2005-200499	B1	20050809		
OS	MARPAT 137:125359				
GI					



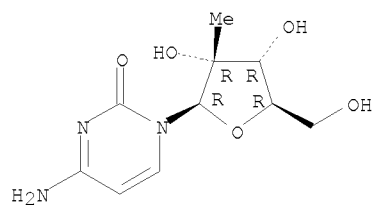
AB The present invention provides the preparation of nucleoside compds. I, wherein B is nucleobase, Y is H, alkylcarbonyl, phosphate; R1 is H, alkenyl, alkynyl, alkyl; R2 and R3 are independently H, OH, halogen, alkyl, alkoxy, alkenyloxy, alkylthio, alkylcarbonyloxy, aryloxy carbonyl, azido, amino, alkylamino; R1 and R2 together with the carbon atom to which they are attached form a 3- to 6-membered heterocycle; R4 is H, OH, SH, NH<sub>2</sub>, alkylamino, cycloalkylamino, halogen, alkyl, alkoxy, CF<sub>3</sub>; R5 and R6 are independently H, hydroxymethyl, Me, fluoromethyl; and certain derivs. thereof which are inhibitors of RNA-dependent RNA viral polymerase. These compds. are inhibitors of RNA-dependent RNA viral replication and are useful for the treatment of RNA-dependent RNA viral infection. They are particularly useful as inhibitors of hepatitis C virus (HCV) NS5B polymerase, as inhibitors of HCV replication, and/or for the treatment of hepatitis C infection. The invention also describes pharmaceutical compns. containing such nucleoside compds. alone or in combination with other agents active against RNA-dependent RNA viral infection, in particular HCV infection. Also disclosed are methods of inhibiting RNA-dependent RNA polymerase, inhibiting RNA-dependent RNA viral replication, and/or treating RNA-dependent RNA viral infection with the nucleoside compds. of the present invention. Thus, 4-amino-1-(2-C-methyl-β-D-ribofuranosyl)-1H-pyrazolo[3,4-d]pyrimidine was prepared as inhibitors of RNA-dependent RNA viral polymerase. Representative compds. tested in the HCV NS5B polymerase assay exhibited IC<sub>50</sub>'s less than 100 μM. The compds. of the present invention were also evaluated for their ability to affect the replication of Hepatitis C Virus RNA in cultured hepatoma (HuH-7) cells containing a sub-genomic HCV Replicon.

IT 20724-73-6P 114262-49-6P 374750-28-4P  
 444019-82-3P 444020-83-1P 444022-03-1P  
 RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of nucleoside derivs. as inhibitors of RNA-dependent human RNA

10/609,298

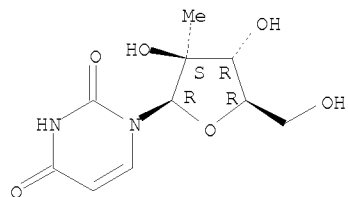
viral polymerase)  
RN 20724-73-6 CAPLUS  
CN Cytidine, 2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry.



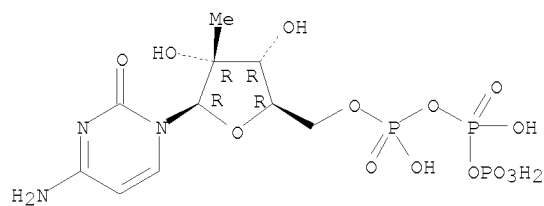
RN 114262-49-6 CAPLUS  
CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-C-methyl-beta-D-arabinofuranosyl)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



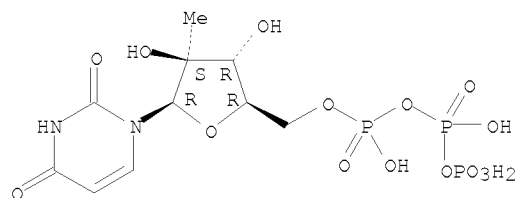
RN 374750-28-4 CAPLUS  
CN Cytidine 5'-(tetrahydrogen triphosphate), 2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry.



RN 444019-82-3 CAPLUS  
CN 2,4(1H,3H)-Pyrimidinedione, 1-[5-O-[hydroxy[[hydroxy(phosphonooxy)phosphinyl]oxy]phosphinyl]-2-C-methyl-beta-D-arabinofuranosyl]- (CA INDEX NAME)

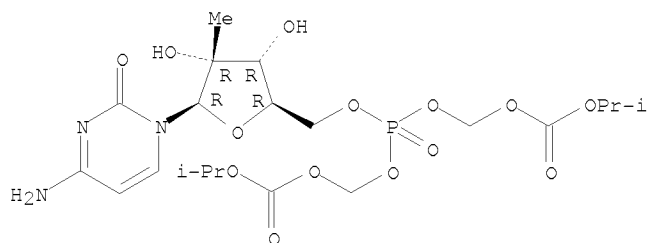
Absolute stereochemistry.



RN 444020-83-1 CAPLUS  
CN 5'-Cytidylic acid, 2'-C-methyl-, bis[[[(1-methylethoxy)carbonyl]oxy]methyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

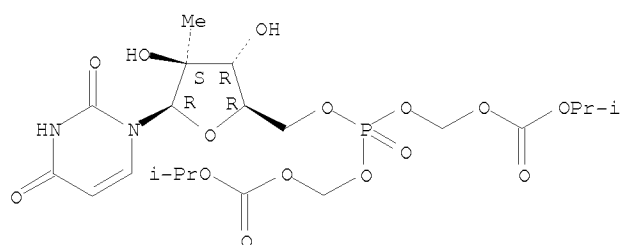
McIntosh



RN 444022-03-1 CAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-[2-C-methyl-5-O-[7-methyl-1-[[[(1-methylethoxy)carbonyl]oxy]methoxy]-1-oxido-5-oxo-2,4,6-trioxa-1-phosphaoct-1-yl]-β-D-arabinofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 57 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2001:886155 CAPLUS

DN 136:590

TI Methods and compositions using modified nucleosides for treating  
flaviviruses and pestiviruses

IN Sommadossi, Jean-Pierre; Lacolla, Paolo

PA Novirio Pharmaceuticals Limited, Cayman I.; Universita Degli Studi Di  
Cagliari

SO PCT Int. Appl., 302 pp.

CODEN: PIXXD2

DT Patent

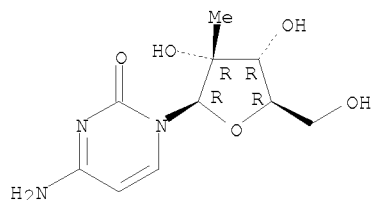
LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001092282	A2	20011206	WO 2001-US16687	20010523
	WO 2001092282	A3	20020502		
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	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
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	EP 1294735	A2	20030326	EP 2001-952131	20010523
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	US 20030060400	A1	20030327	US 2001-863816	20010523
	US 6812219	B2	20041102		
	CN 1468249	A	20040114	CN 2001-813182	20010523
	BR 2001011196	A	20040406	BR 2001-11196	20010523
	JP 2004510698	T	20040408	JP 2002-500895	20010523
	NZ 536570	A	20060831	NZ 2001-536570	20010523
	EP 1736478	A1	20061227	EP 2006-75198	20010523
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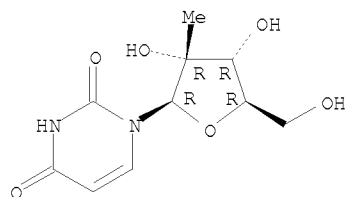
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NO 2002005600	A	20030117	NO 2002-5600	20021121
MX 2002PA11691	A	20040517	MX 2002-PA11691	20021126
IN 2002DN01187	A	20070309	IN 2002-DN1187	20021202
ZA 2002010112	A	20040623	ZA 2002-10112	20021212
US 20040063622	A1	20040401	US 2003-602693	20030620
US 7148206	B2	20061212		
US 20040097462	A1	20040520	US 2003-602692	20030620
US 7101861	B2	20060905		
US 20040102414	A1	20040527	US 2003-602694	20030620
US 7105493	B2	20060912		
US 20060166865	A1	20060727	US 2003-602135	20030620
US 7163929	B2	20070116		
US 20070037773	A1	20070215	US 2006-527124	20060925
AU 2007202602	A1	20070719	AU 2007-202602	20070607
KR 2008021797	A	20080307	KR 2008-701618	20080121
PRAI US 2000-207674P	P	20000526		
US 2001-283276P	P	20010411		
CN 2001-813182	A3	20010523		
EP 2001-952131	A3	20010523		
US 2001-863816	A3	20010523		
WO 2001-US16687	W	20010523		
KR 2002-715794	A3	20021122		
US 2003-602135	A1	20030620		
OS MARPAT 136:590				
AB A method and composition are provided for treating a host infected with flavivirus or pestivirus, comprising administering an effective amount of a 1', 2' or 3'-modified nucleoside or a pharmaceutically acceptable salt or prodrug thereof.				
IT 20724-73-6 31448-54-1 119410-84-3				
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (nucleoside derivs. for treating flaviviruses and pestiviruses)				
RN 20724-73-6 CAPLUS				
CN Cytidine, 2'-C-methyl- (CA INDEX NAME)				

Absolute stereochemistry.



RN 31448-54-1 CAPLUS  
 CN Uridine, 2'-C-methyl- (CA INDEX NAME)

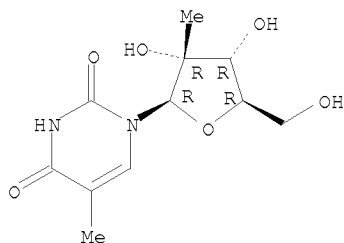
Absolute stereochemistry. Rotation (+).



RN 119410-84-3 CAPLUS  
 CN Uridine, 5-methyl-2'-C-methyl- (9CI) (CA INDEX NAME)

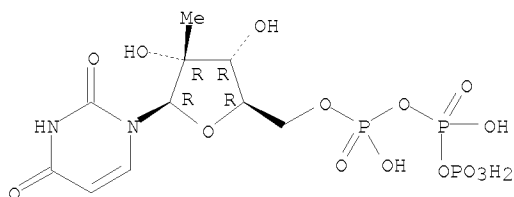
Absolute stereochemistry. Rotation (+).

10/609,298



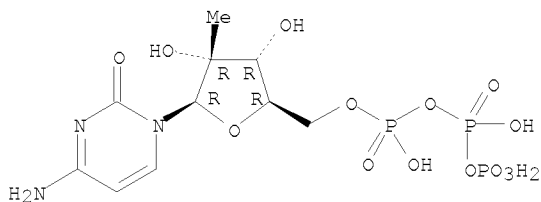
IT 125911-76-4 374750-28-4  
RL: BSU (Biological study, unclassified); PKT (Pharmacokinetics); BIOL  
(Biological study)  
(nucleoside derivs. for treating flaviviruses and  
pestiviruses)  
RN 125911-76-4 CAPLUS  
CN Uridine 5'-(tetrahydrogen triphosphate), 2'-C-methyl- (9CI) (CA INDEX  
NAME)

Absolute stereochemistry.



RN 374750-28-4 CAPLUS  
CN Cytidine 5'-(tetrahydrogen triphosphate), 2'-C-methyl- (CA INDEX NAME)

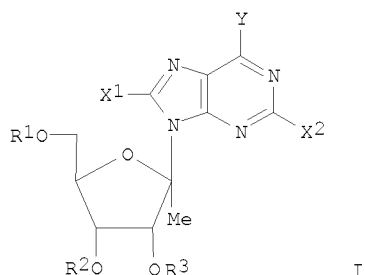
Absolute stereochemistry.



L6 ANSWER 58 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN  
AN 2001:868467 CAPLUS  
DN 136:6296  
TI Preparation of antiviral nucleosides and methods for treating  
hepatitis C virus  
IN Sommadossi, Jean-Pierre; Lacolla, Paulo  
PA Novirio Pharmaceuticals Limited, Cayman I.; Universita degli Studi di  
Cagliari  
SO PCT Int. Appl., 296 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1  
PATENT NO. KIND DATE APPLICATION NO. DATE  
PI WO 2001090121 A2 20011129 WO 2001-US16671 20010523  
WO 2001090121 A3 20020502  
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,

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	RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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AU	2001074906	A	20011203	AU 2001-74906	20010523
US	20030050229	A1	20030313	US 2001-864078	20010523
US	6914054	B2	20050705		
EP	1292603	A2	20030319	EP 2001-941564	20010523
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JP	2004533401	T	20041104	JP 2001-586308	20010523
NZ	522863	A	20050729	NZ 2001-522863	20010523
EP	1669364	A2	20060614	EP 2006-75216	20010523
EP	1669364	A3	20060913		
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NO	325352	B1	20080407		
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US	20040101535	A1	20040527	US 2003-602976	20030620
US	7169766	B2	20070130		
US	20050124532	A1	20050609	US 2003-602142	20030620
US	20050137161	A1	20050623	US 2003-602136	20030620
US	7157441	B2	20070102		
AU	2006203121	A1	20060810	AU 2006-203121	20060721
AU	2006203122	A1	20060810	AU 2006-203122	20060721
KR	2007036806	A	20070403	KR 2007-706401	20070320
NO	2007003151	A	20030106	NO 2007-3151	20070620
IN	2007DN09886	A	20080125	IN 2007-DN9886	20071219
IN	2007DN09890	A	20080125	IN 2007-DN9890	20071219
IN	2007DN09896	A	20080208	IN 2007-DN9896	20071219
KR	2008030670	A	20080404	KR 2008-703747	20080215
PRAI	US 2000-206585P	P	20000523		
	AU 2001-74906	A3	20010523		
	EP 2001-941564	A3	20010523		
	NZ 2001-522863	A3	20010523		
	US 2001-864078	A1	20010523		
	WO 2001-US16671	W	20010523		
	KR 2002-715790	A3	20021122		
	NO 2002-5627	A	20021122		
	IN 2002-DN1184	A3	20021202		
OS	MARPAT 136:6296				
GI					



AB A method and composition for treating a host infected with hepatitis C comprising administering an effective hepatitis C treatment amount of a described 1'-, 2'- or 3'-modified

nucleosides I, wherein : R1-R3 and R are independently H, phosphate (including mono, di- or triphosphate and a stabilized phosphate prodrug); acyl; alkyl; sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the Ph group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered in vivo is capable of providing a compound wherein R1-R3 are independently H or phosphate; Y is hydrogen, bromo, chloro, fluoro, iodo, OR4, NR4R5 or SR4; X1 and X2 are independently selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR4, NR4R5 or SR4; and R4 and R5 are independently hydrogen, acyl, alkyl, or a pharmaceutically acceptable salt or prodrug thereof, is provided. Thus, I (R1-R3 = X1 = X2 = H, Y = NH2) was prepared and tested in Cynomolgus monkeys as antiviral agent. Oral bioavailability in monkeys, bone human bone marrow toxicity (IC50 > 10  $\mu$ M), and mitochondrial toxicity, were reported .

IT 20724-73-6P 31448-54-1P 119410-84-3P  
125911-76-4P 374750-28-4P

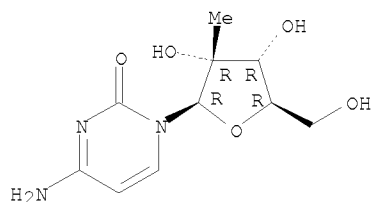
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of antiviral nucleosides and methods for treating hepatitis C virus)

RN 20724-73-6 CAPLUS

CN Cytidine, 2'-C-methyl- (CA INDEX NAME)

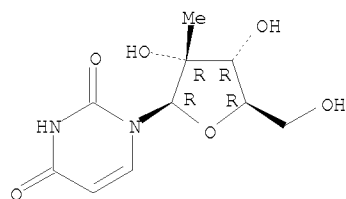
Absolute stereochemistry.



RN 31448-54-1 CAPLUS

CN Uridine, 2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

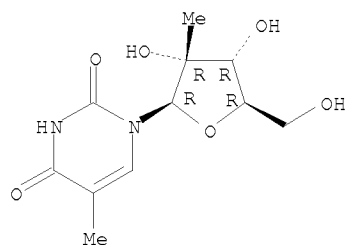


RN 119410-84-3 CAPLUS

CN Uridine, 5-methyl-2'-C-methyl- (9CI) (CA INDEX NAME)

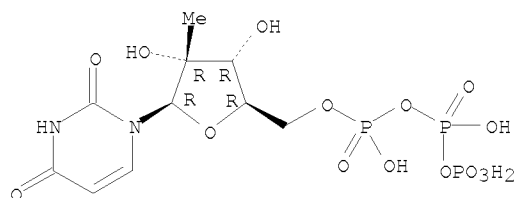
Absolute stereochemistry. Rotation (+).

10/609,298



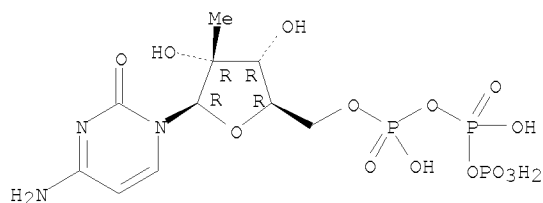
RN 125911-76-4 CAPLUS  
CN Uridine 5'-(tetrahydrogen triphosphate), 2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 374750-28-4 CAPLUS  
CN Cytidine 5'-(tetrahydrogen triphosphate), 2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry.



=> file reg		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	132.83	311.40
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-15.20	-15.20

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provided by InfoChem.

STRUCTURE FILE UPDATES: 6 JUN 2008 HIGHEST RN 1026208-38-7  
DICTIONARY FILE UPDATES: 6 JUN 2008 HIGHEST RN 1026208-38-7

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conducting SmartSELECT searches.

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<http://www.cas.org/support/stngen/stndoc/properties.html>

=>

Uploading C:\Program Files\Stnexp\Queries\10609298b.str

L7           STRUCTURE UPLOADED

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L7 HAS NO ANSWERS

L7           STR

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

Structure attributes must be viewed using STN Express query preparation.

=> s l7

SAMPLE SEARCH INITIATED 18:14:14 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED -       2232 TO ITERATE

89.6% PROCESSED       2000 ITERATIONS                   4 ANSWERS  
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)  
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:   ONLINE   \*\*COMPLETE\*\*  
                          BATCH    \*\*COMPLETE\*\*  
PROJECTED ITERATIONS:       41806 TO   47474  
PROJECTED ANSWERS:           4 TO       215

L8           4 SEA SSS SAM L7

=> s l7 full

FULL SEARCH INITIATED 18:14:19 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED -       44523 TO ITERATE

100.0% PROCESSED       44523 ITERATIONS               171 ANSWERS  
SEARCH TIME: 00.00.01

L9           171 SEA SSS FUL L7

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	178.36	489.76

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-15.20

FILE 'CAPLUS' ENTERED AT 18:14:23 ON 08 JUN 2008  
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FILE COVERS 1907 - 8 Jun 2008 VOL 148 ISS 24

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10/609,298

FILE LAST UPDATED: 6 Jun 2008 (20080606/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.  
They are available for your review at:

<http://www.cas.org/legal/infopolicy.html>

=> s 19

L10 74 L9

=> s 110 and (flavivirus or pestivirus or flaviviridae or hcv or hepatitis c)

1747 FLAVIVIRUS

864 FLAVIVIRUSES

2025 FLAVIVIRUS

(FLAVIVIRUS OR FLAVIVIRUSES)

501 PESTIVIRUS

266 PESTIVIRUSES

597 PESTIVIRUS

(PESTIVIRUS OR PESTIVIRUSES)

645 FLAVIVIRIDAE

14183 HCV

24 HCVS

14187 HCV

(HCV OR HCVS)

67218 HEPATITIS

1 HEPATITISES

67218 HEPATITIS

(HEPATITIS OR HEPATITISES)

3835463 C

20967 HEPATITIS C

(HEPATITIS(W)C)

L11 37 L10 AND (FLAVIVIRUS OR PESTIVIRUS OR FLAVIVIRIDAE OR HCV OR HEPATITIS C)

=> d bib abs hitstr 1-37

L11 ANSWER 1 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2008:562068 CAPLUS

DN 148:509492

TI The hepatitis C virus replicon presents a higher  
barrier to resistance to nucleoside analogs than to nonnucleoside  
polymerase or protease inhibitors

AU McCown, Matthew F.; Rajyaguru, Sonal; Le Pogam, Sophie; Ali, Samir; Jiang,  
Wen-Rong; Kang, Hyunsoon; Symons, Julian; Cammack, Nick; Najera, Isabel

CS Department of HCV Biology, Virology Disease Biology Area, Roche Palo Alto  
LLC, Palo Alto, CA, 94304, USA

SO Antimicrobial Agents and Chemotherapy (2008), 52(5), 1604-1612  
CODEN: AMACQ; ISSN: 0066-4804

PB American Society for Microbiology

DT Journal

LA English

AB Specific inhibitors of hepatitis C virus (HCV

) replication that target the NS3/4A protease (e.g., VX-950) or the NS5B  
polymerase (e.g., R1479/R1626, PSI-6130/R7128, NM107/NM283, and  
HCV-796) have advanced into clin. development. Treatment of  
patients with VX-950 or HCV-796 rapidly selected for  
drug-resistant variants after a 14-day monotherapy treatment period.  
However, no viral resistance was identified after monotherapy with R1626  
(prodrug of R1479) or NM283 (prodrug of NM107) after 14 days of  
monotherapy. Based upon the rapid selection of resistance to the protease  
and nonnucleoside inhibitors during clin. trials and the lack of selection  
of resistance to the nucleoside inhibitors, we used the replicon system to  
determine whether nucleoside inhibitors demonstrate a higher genetic barrier to  
resistance than protease and nonnucleoside inhibitors. Treatment of  
replicon cells with nucleoside inhibitors at 10 and 15 times the 50%  
effective concentration resulted in clearance of the replicon, while treatment  
with a nonnucleoside or protease inhibitor selected resistant colonies.  
In combination, the presence of a nucleoside inhibitor reduced the  
frequency of colonies resistant to the other classes of inhibitors. These  
results indicate that the HCV replicon presents a higher barrier  
to the selection of resistance to nucleoside inhibitors than to  
nonnucleoside or protease inhibitors. Furthermore, the combination of a  
nonnucleoside or protease inhibitor with a nucleoside polymerase inhibitor

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could have a clear clin. benefit through the delay of resistance emergence.

IT 640725-71-9, NM283

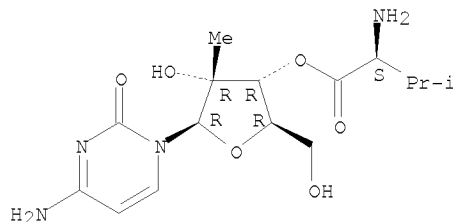
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(hepatitis C virus replicon presents a higher barrier to resistance to nucleoside analogs than to nonnucleoside polymerase or protease inhibitors)

RN 640725-71-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



● 2 HCl

RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2008:416659 CAPLUS

DN 148:417879

TI Compositions of immunostimulatory oligonucleotides as Toll-like receptor ligands and antiviral agents for therapeutic administration

IN Vollmer, Jorg; Jurk, Marion; Uhlmann, Eugen; Debelak, Harald; Bratzler, Robert L.; Vicari, Alain

PA Coley Pharmaceutical Group, Inc., USA; Coley Pharmaceutical G.m.b.H.; Coley Pharmaceutical Group, Ltd.

SO PCT Int. Appl., 89pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

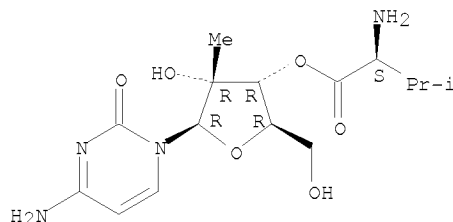
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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	RW:				
	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRAI US 2006-847408P P 20060927

AB The invention relates to methods and products for the treatment of viral infection using a combination of antiviral agents and Toll-like receptor (TLR) ligands. The TLR ligands comprise immunostimulatory oligonucleotides, preferably containing modifications selected from 8-oxo-rG, 8-bromo-dG, 8-bromo-dA, and isatoribine (Immunosine) with a 5'-5' linkage. The 8-modified guanine residues enhance immunostimulatory activity, particularly when present at the 5' end of the oligonucleotide. Combination of Ribavirin with an immunostimulatory CpG-containing oligonucleotide results in a decrease of interleukin-10 relative to interferon- $\alpha$  inducing activity. Further, Ribavirin and CpG

oligonucleotide improve survival in a mouse cancer model.  
 IT 640281-90-9, Valopicitabine  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (compns. of immunostimulatory oligonucleotides as Toll-like receptor  
 ligands and antiviral agents for therapeutic administration)  
 RN 640281-90-9 CAPLUS  
 CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L11 ANSWER 3 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2008:352859 CAPLUS

DN 148:394354

TI Compositions and methods for treatment of viral diseases

IN Johansen, Lisa M.; Owens, Christopher M.; Mawhinney, Christina; Chappell,  
 Todd W.; Brown, Alexander T.; Frank, Michael G.; Altmeyer, Ralf

PA Combinatorx (Singapore) Pre. Ltd., Singapore

SO PCT Int. Appl., 237pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

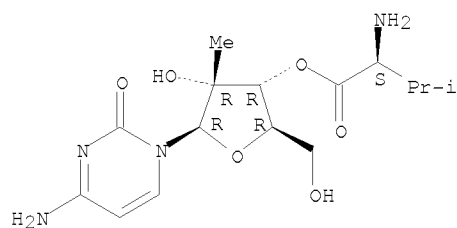
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008033466	A2	20080320	WO 2007-US19932	20070913
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM PRAI US 2006-844463P P 20060914 US 2006-874061P P 20061211				

AB Based on the results of the authors screen identifying compds. and  
 combinations of compds. having antiviral activity, the present invention  
 features compns., methods, and kits useful in the treatment of viral  
 diseases. In certain embodiments, the viral disease is caused by a single  
 stranded RNA virus, a flaviviridae virus, or a hepatic virus.  
 In particular embodiments, the viral disease is viral hepatitis (e.g.,  
 hepatitis A, hepatitis B, hepatitis C, hepatitis D,  
 hepatitis E). Also featured are screening methods for identification of  
 novel compds. that may be used to treat a viral disease.

IT 640281-90-9, Valopicitabine 640725-71-9, NM-283  
 1015079-99-8 1015080-00-8 1015080-23-5  
 1015080-28-0 1015080-31-5 1015080-38-2  
 1015080-56-4 1015080-58-6 1015080-59-7  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (compns. and methods for treatment of viral diseases)  
 RN 640281-90-9 CAPLUS  
 CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

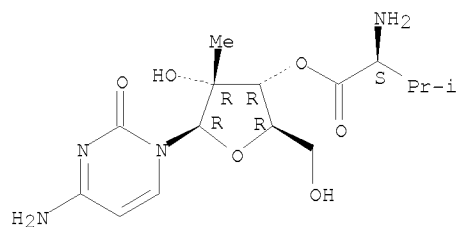
Absolute stereochemistry. Rotation (+).

10/609,298



RN 640725-71-9 CAPLUS  
CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA  
INDEX NAME)

Absolute stereochemistry. Rotation (+).



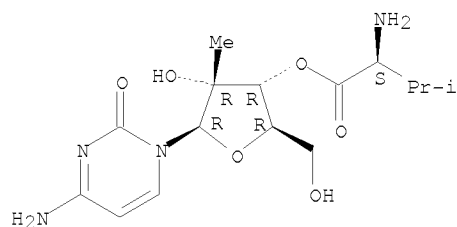
● 2 HCl

RN 1015079-99-8 CAPLUS  
CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2), mixt.  
with (3R,5aS,6R,8aS,9R,12S,12aR)-octahydro-3,6,9-trimethyl-3,12-epoxy-12H-  
pyrano[4,3-j]-1,2-benzodioxepin-10(3H)-one (CA INDEX NAME)

CM 1

CRN 640725-71-9  
CMF C15 H24 N4 O6 . 2 Cl H

Absolute stereochemistry. Rotation (+).



● 2 HCl

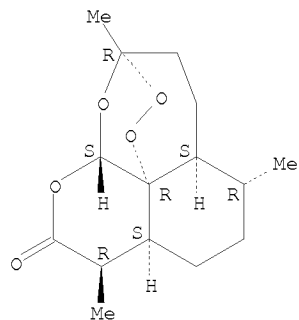
CM 2

CRN 63968-64-9  
CMF C15 H22 O5

Absolute stereochemistry.

McIntosh

10/609,298

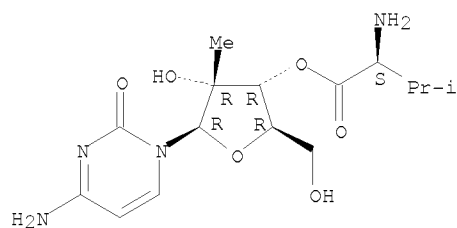


RN 1015080-00-8 CAPLUS  
CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2), mixt.  
with 1,8,9-trihydroxy-3-methoxy-6H-benzofuro[3,2-c][1]benzopyran-6-one  
(CA INDEX NAME)

CM 1

CRN 640725-71-9  
CMF C15 H24 N4 O6 . 2 Cl H

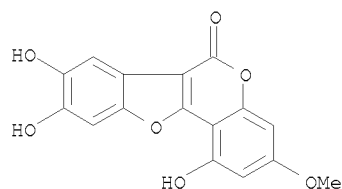
Absolute stereochemistry. Rotation (+).



● 2 HCl

CM 2

CRN 524-12-9  
CMF C16 H10 O7



RN 1015080-23-5 CAPLUS  
CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2), mixt.  
with (6E)-N-[(4-hydroxy-3-methoxyphenyl)methyl]-8-methyl-6-nonenamide (CA  
INDEX NAME)

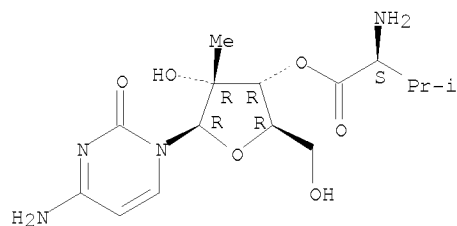
CM 1

CRN 640725-71-9  
CMF C15 H24 N4 O6 . 2 Cl H

Absolute stereochemistry. Rotation (+).

McIntosh

10/609,298



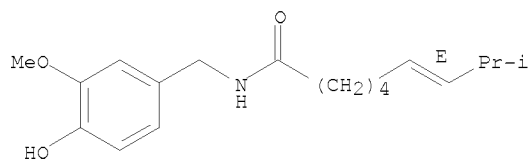
● 2 HCl

CM 2

CRN 404-86-4

CMF C18 H27 N O3

Double bond geometry as shown.



RN 1015080-28-0 CAPLUS

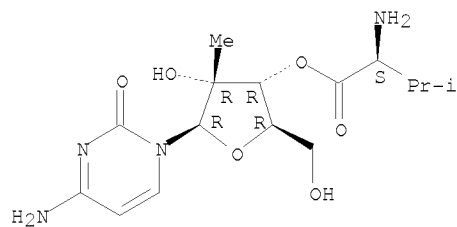
CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2), mixt.  
with 3-[(3,5-dibromo-4-hydroxyphenyl)methylene]-1,3-dihydro-5-iodo-2H-  
indol-2-one (CA INDEX NAME)

CM 1

CRN 640725-71-9

CMF C15 H24 N4 O6 . 2 Cl H

Absolute stereochemistry. Rotation (+).



● 2 HCl

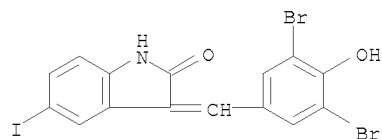
CM 2

CRN 220904-83-6

CMF C15 H8 Br2 I N O2

McIntosh

10/609,298



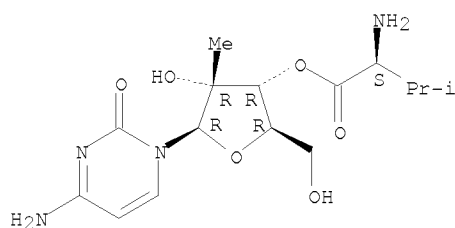
RN 1015080-31-5 CAPLUS  
CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2), mixt.  
with 2,3,6,7-tetrahydro-9,10-dimethoxy-3-methyl-2-[(2,4,6-trimethylphenyl)imino]-4H-pyrimido[6,1-a]isoquinolin-4-one (CA INDEX NAME)

CM 1

CRN 640725-71-9

CMF C15 H24 N4 O6 . 2 Cl H

Absolute stereochemistry. Rotation (+).

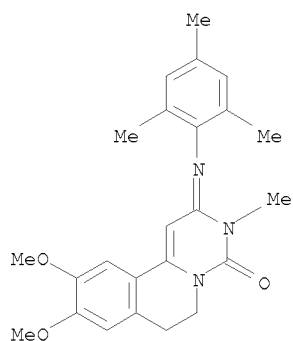


● 2 HCl

CM 2

CRN 79855-88-2

CMF C24 H27 N3 O3



RN 1015080-38-2 CAPLUS  
CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2), mixt.  
with 2,3-dihydro-2-hydroxy-4H-1-benzopyran-4-one (CA INDEX NAME)

CM 1

CRN 640725-71-9

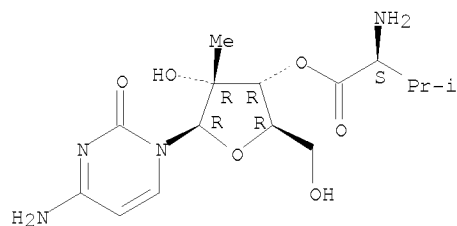
CMF C15 H24 N4 O6 . 2 Cl H

Absolute stereochemistry. Rotation (+).

McIntosh



10/609,298

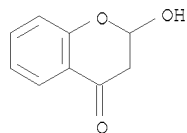


● 2 HCl

CM 2

CRN 57669-32-6

CMF C9 H8 O3



RN 1015080-56-4 CAPLUS

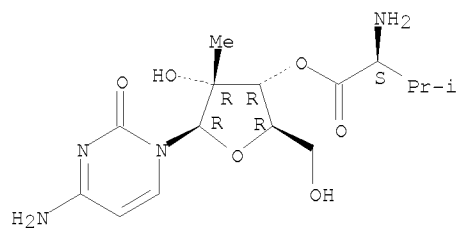
CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2), mixt.  
with 1-(4-fluorophenyl)-4-[4-hydroxy-4-[3-(trifluoromethyl)phenyl]-1-  
piperidinyl]-1-butanone (CA INDEX NAME)

CM 1

CRN 640725-71-9

CMF C15 H24 N4 O6 . 2 Cl H

Absolute stereochemistry. Rotation (+).



● 2 HCl

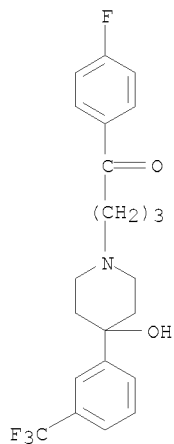
CM 2

CRN 749-13-3

CMF C22 H23 F4 N O2

McIntosh

10/609,298



RN 1015080-58-6 CAPLUS

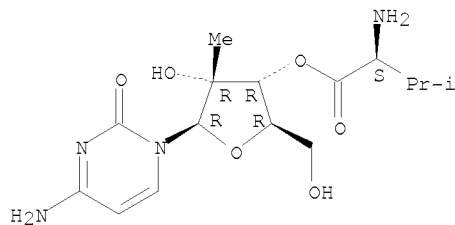
CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2), mixt.  
with 3-(2-phenyldiazenyl)-2,6-pyridinediamine (CA INDEX NAME)

CM 1

CRN 640725-71-9

CMF C15 H24 N4 O6 . 2 Cl H

Absolute stereochemistry. Rotation (+).

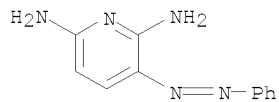


● 2 HCl

CM 2

CRN 94-78-0

CMF C11 H11 N5



RN 1015080-59-7 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2), mixt.  
with  $\alpha,\alpha,\alpha$ -trifluorothymidine (CA INDEX NAME)

CM 1

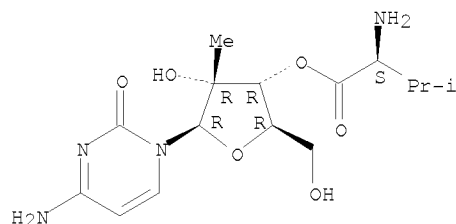
CRN 640725-71-9

CMF C15 H24 N4 O6 . 2 Cl H

Absolute stereochemistry. Rotation (+).

McIntosh

10/609,298



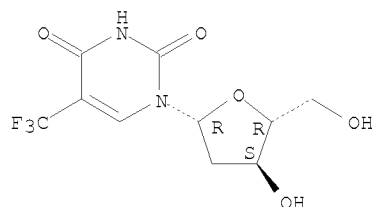
● 2 HCl

CM 2

CRN 70-00-8

CMF C10 H11 F3 N2 O5

Absolute stereochemistry.



L11 ANSWER 4 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2008:90893 CAPLUS

DN 148:192198

TI Preparation of peptidomimetics as modulators of pharmacokinetic properties of therapeutics by inhibiting cytochrome P450 monooxygenase

IN Desai, Manoj C.; Hong, Allen Yu; Liu, Hongtao; Xu, Lianhong; Vivian, Randall W.

PA Gilead Sciences, Inc., USA

SO PCT Int. Appl., 346pp.

CODEN: PIXXD2

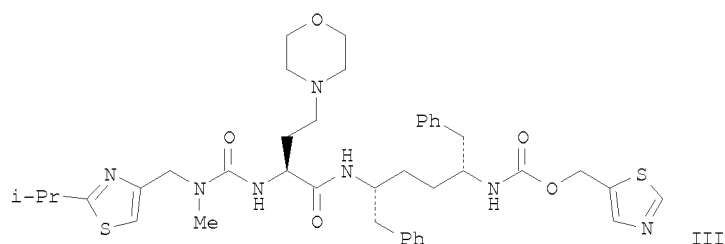
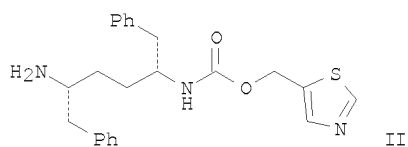
DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2008010921	A2	20080124	WO 2007-US15604	20070706
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
	RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	US 20080108617	A1	20080508	US 2007-825605	20070706
PRAI	US 2006-819315P	P	20060707		
	US 2006-832371P	P	20060721		
	US 2007-903228P	P	20070223		
OS	MARPAT 148:192198				
GI					

McIntosh

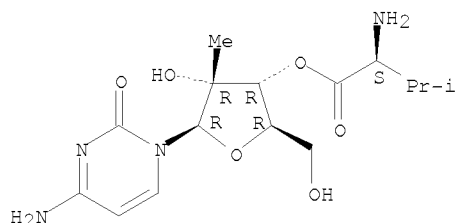


AB The invention is related to the preparation of  $R_8YZ_1[CONR_1(CR_2R_2)_m]nL_1NR_3CH[L_3A(L_4Ar)p]CHR_4L_2CH[L_3A(L_4Ar)p]NR_5COZ_2XR_9$  [I;  $L_1 = C(R_6)_2$ , CO,  $SO_2$ , NHCO and derivs., OCO;  $R_4, R_6 =$  independently H, heteroalkyl, (un)substituted alkyl;  $L_2 =$  a covalent bond,  $C(R_6)_2$ , CO; each  $L_3 =$  independently a covalent bond, (un)substituted alkylene; each  $L_4 = L_3$ , O,  $CH_2O$ , NH; each A = H, (un)substituted alkyl, aryl, heterocyclyl with the proviso that when A = H,  $p = 0$ ;  $Z_1, Z_2 =$  independently O, NH and derivs.; Y, X = independently heterocyclyl, heterocyclylalkyl; each Ar = independently (un)substituted (hetero)aryl;  $R_1, R_3, R_5 =$  independently H, (un)substituted aryl/alkyl; each  $R_2 =$  independently H, (un)substituted arylhetero/hydroxy/amino/alkyl, alkylene-CO $_2$ H, alkylene-CO-alkyl, etc.;  $R_8, R_9$  are each one or more H's or substituents selected from Cl, CN, (un)substituted alkyl, aryl, heterocyclyl;  $m = 1-2$ ;  $n = 0-1$ ; each  $p =$  independently 0-1], their pharmaceutically acceptable salts, solvates and esters, and compns. containing them which improve the pharmacokinetics of a co-administered drug which is metabolized by cytochrome P 450 monooxygenase. Thus, a multi-step synthesis using 2-isopropyl-4-[(methylamino)methyl]-1,3-thiazole, (2S)-2-amino-4-[(tert-butoxycarbonyl)amino]butanoic acid Me ester, amine II and  $(BrCH_2CH_2)_2O$  was given for III. III inhibited CYP450 3A4 ( $IC_{50} = 80-150$  nM), CYP450 2C9 ( $IC_{50} = 1,000-10,000$  nM) and protease ( $EC_{50} > 20,000$  nM in an anti HIV-1 cell culture assay). I alone or in combination with one or more addnl. therapeutic agents which are metabolized by cytochrome P 450 monooxygenase are useful for treating a viral infection, e.g. HIV (no data).

IT 640281-90-9, Valopicitabine 640725-71-9, NM-283  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (compds. as modulators of pharmacokinetic properties of therapeutic agents)

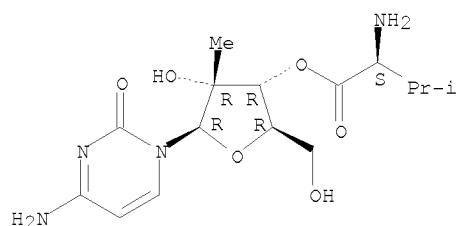
RN 640281-90-9 CAPLUS  
 CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 640725-71-9 CAPLUS  
 CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA INDEX NAME)

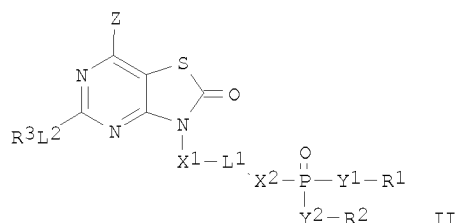
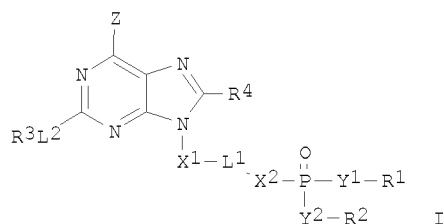
Absolute stereochemistry. Rotation (+).



● 2 HCl

L11 ANSWER 5 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN  
 AN 2008:40914 CAPLUS  
 DN 148:168504  
 TI Preparation of purine and thiadeazapurine phosphonate derivatives as  
 modulators of toll-like receptor 7  
 IN Chong, Lee S.; Desai, Manoj C.; Gallagher, Brian; Graupe, Michael;  
 Halcomb, Randall L.; Yang, Hong; Zhang, Jennifer R.  
 PA Gilead Sciences, Inc., USA  
 SO PCT Int. Appl., 273pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2008005555	A1	20080110	WO 2007-US15615	20070706
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	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	US 20080008682	A1	20080110	US 2007-825377	20070706
PRAI	US 2006-819490P	P	20060707		
	US 2006-832851P	P	20060724		
OS	MARPAT 148:168504				
GI					



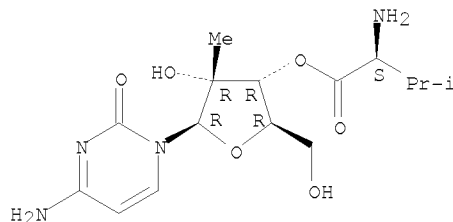
AB The present application provides for a compound I [Z = OH, NH<sub>2</sub>; X<sub>1</sub> = (un)substituted alkylene, alkenylene, alkynylene, carbocyclylene, heterocyclylene; L<sub>1</sub> = bond, (un)substituted arylene, heterocyclylene, carbocyclylene, S, S(:O), SO<sub>2</sub>, NR<sub>5</sub>, O; X<sub>2</sub> = bond, (un)substituted alkylene; L<sub>2</sub> = NR<sub>5</sub>, NR<sub>5</sub>C(:O), O, S, S(:O), SO<sub>2</sub>, bond; R<sub>3</sub> = H, (un)substituted alkyl, heteroalkyl, alkenyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl; Y<sub>1</sub>, Y<sub>2</sub> = bond, O, NR<sub>5</sub>, Y<sub>1</sub>R<sub>1</sub>, Y<sub>2</sub>R<sub>2</sub> = ON:CR<sub>6</sub>R<sub>7</sub>; R<sub>1</sub>, R<sub>2</sub> = H, (un)substituted alkyl, carbocyclyl, heterocyclyl, alkenyl, alkynyl, arylalkyl, etc.; R<sub>4</sub> = H, halogen, OH, O-alkyl, O-alkylene-OCO<sub>2</sub>R<sub>5</sub>, OCO<sub>2</sub>R<sub>5</sub>, SH, NHR<sub>5</sub>; R<sub>5</sub>, R<sub>6</sub>, R<sub>7</sub> = H, (un)substituted alkyl, carbocyclyl, heterocyclyl, alkenyl, alkynyl, arylalkyl, heterocyclylalkyl, etc.] or II or a pharmaceutically acceptable salt, solvate, and/or ester thereof, compds. containing such compds., therapeutic methods that include the administration of such compds., and therapeutic methods that include the administration of such compds. with at least one addnl. active agent. Thus, [(3-((6-amino-8-hydroxy-2-(2-methoxyethoxy)-9H-purin-9-yl)methyl)phenyl)methyl](methyl)phosphinic acid [I; Z = NH<sub>2</sub>, R<sub>4</sub> = OH, L<sub>2</sub> = O, R<sub>3</sub> = CH<sub>2</sub>CH<sub>2</sub>OMe, X<sub>1</sub> = X<sub>2</sub> = CH<sub>2</sub>, L<sub>1</sub> = 1,3-phenylene, Y<sub>1</sub>R<sub>1</sub> = Me, Y<sub>2</sub>R<sub>2</sub> = OH] was prepared from 6-chloroadenine via N-alkylation with 3-(BrCH<sub>2</sub>)C<sub>6</sub>H<sub>4</sub>CO<sub>2</sub>Me, alkoxylation with MeOCH<sub>2</sub>CH<sub>2</sub>OH, reesterification with MeI, bromination with Br<sub>2</sub>, Dibal-H reduction, methanolysis with NaOMe/MeOH, acid hydrolysis, bromination with PBr<sub>3</sub>, phosphorylation with MeP(OEt)<sub>2</sub> and acid hydrolysis under microwave irradiation. The toll-like receptor 7 modulating activity of I and II were investigated (no data).

IT 640281-90-9, Valopicitabine 640725-71-9, NM-283  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (compds. as modulators of Toll-like receptor 7 useful in combination therapy and prevention of TLR7 activation-related diseases)

RN 640281-90-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



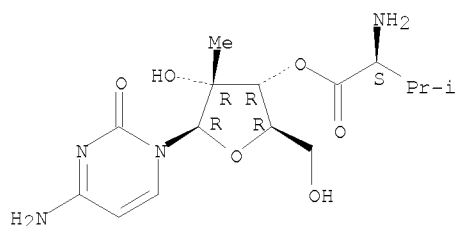
RN 640725-71-9 CAPLUS

McIntosh

10/609,298

CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA  
INDEX NAME)

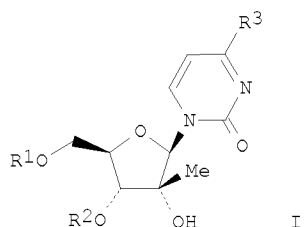
Absolute stereochemistry. Rotation (+).



● 2 HCl

L11 ANSWER 6 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN  
AN 2007:1332915 CAPLUS  
DN 148:11439  
TI 2'-C-Methyl-Ribofuranosyl Cytidine Prodrugs, Pharmaceutical Compositions  
and Uses Thereof  
IN Gallop, Mark A.  
PA USA  
SO U.S. Pat. Appl. Publ., 59pp.  
CODEN: USXXCO  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 20070270374	A1	20071122	US 2007-752214	20070522
PRAI	US 2006-808360P	P	20060522		
OS	MARPAT 148:11439				
GI					



AB The present disclosure provides the preparation of 2'-C-methyl-ribofuranosyl cytidine prodrugs I, wherein R1 and R2 are independently H, acyl, acyloxyalkylcarbonyl, oxycarbonyl, substituted aminocarbonyl; R3 is substituted imine, substituted amine, and pharmaceutical compns. thereof to treat viral diseases such as hepatitis C. Thus,  $\beta$ -(4-allyloxycarbonylamino-2-oxo-1H-pyrimidin-1-yl)-2-C-methylribofuranose was prepared (no data) and tested in vitro in combination with antiviral agents to treat viral diseases, wherein the second antiviral agent is selected from an interferon, ribavirin, interleukin, an NS3 protease inhibitor, cysteine protease inhibitor, thiazolidine derivative, thiazolidine, benzanilide, phenanthrenequinone, a helicase inhibitor, a polymerase inhibitor, a nucleotide analog, gliotoxin, cerulenin, antisense phosphorothioate oligodeoxyribonucleotides, inhibitor of IRES-dependent translation, and a ribozyme. In vitro compound transport assays with CNT1, CNT2, CNT3, ENT1 and ENT2 expressing cells, are claimed.

IT 957687-30-8P 957687-34-2P 957687-53-5P  
957687-55-7P 957687-58-0P 957687-62-6P  
957687-64-8P 957687-83-1P

McIntosh

10/609,298

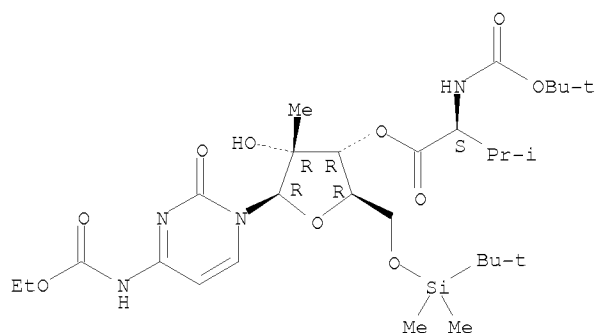
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(2'-C-methyl-ribofuranosyl cytidine prodrugs, pharmaceutical compns. and uses thereof)

RN 957687-30-8 CAPLUS

CN L-Valine, N-[(1,1-dimethylethoxy)carbonyl]-, 3'-ester with 5'-O-[(1,1-dimethylethyl)dimethylsilyl]-N-(ethoxycarbonyl)-2'-C-methylcytidine (CA INDEX NAME)

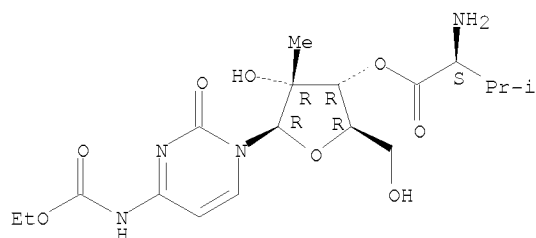
Absolute stereochemistry.



RN 957687-34-2 CAPLUS

CN L-Valine, 3'-ester with N-(ethoxycarbonyl)-2'-C-methylcytidine (CA INDEX NAME)

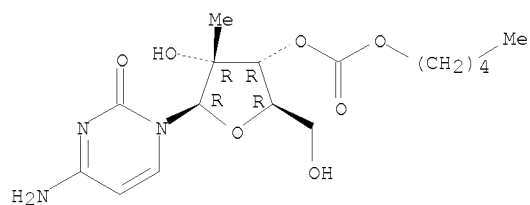
Absolute stereochemistry.



RN 957687-53-5 CAPLUS

CN Cytidine, 2'-C-methyl-, 3'-(pentyl carbonate) (CA INDEX NAME)

Absolute stereochemistry.



RN 957687-55-7 CAPLUS

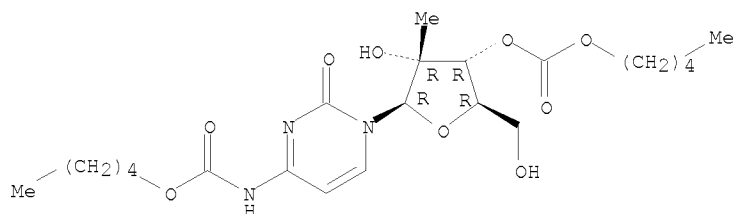
CN Cytidine, 2'-C-methyl-N-[(pentyloxy)carbonyl]-, 3'-(pentyl carbonate) (CA INDEX NAME)

Absolute stereochemistry.

McIntosh

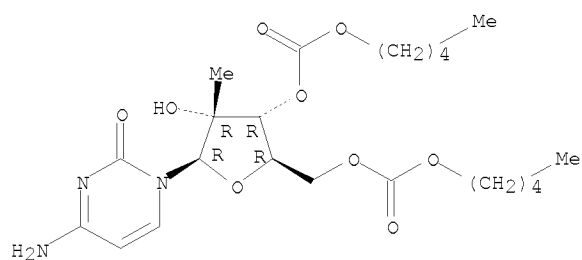


10/609,298



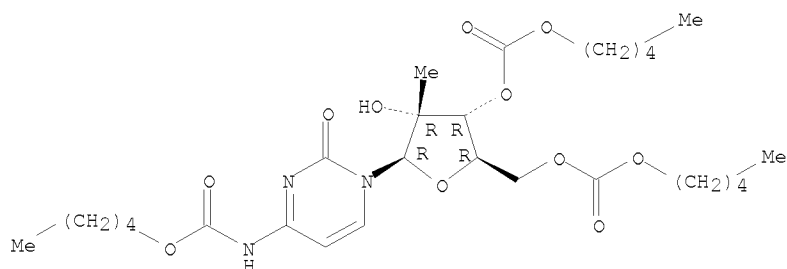
RN 957687-58-0 CAPLUS  
CN Cytidine, 2'-C-methyl-, 3',5'-bis(pentyl carbonate) (CA INDEX NAME)

Absolute stereochemistry.



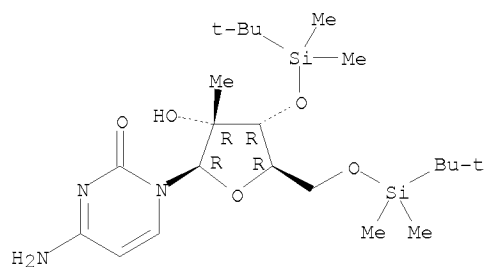
RN 957687-62-6 CAPLUS  
CN Cytidine, 2'-C-methyl-N-[(pentyloxy)carbonyl]-, 3',5'-bis(pentyl carbonate) (CA INDEX NAME)

Absolute stereochemistry.



RN 957687-64-8 CAPLUS  
CN Cytidine, 3',5'-bis-O-[(1,1-dimethylethyl)dimethylsilyl]-2'-C-methyl- (CA INDEX NAME)

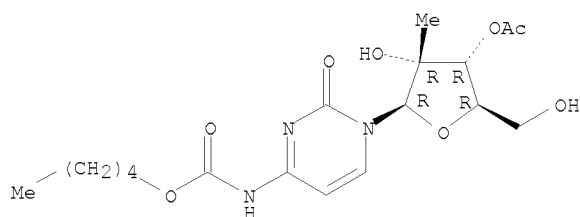
Absolute stereochemistry.



RN 957687-83-1 CAPLUS  
CN Cytidine, 2'-C-methyl-N-[(pentyloxy)carbonyl]-, 3'-acetate (CA INDEX NAME)

McIntosh

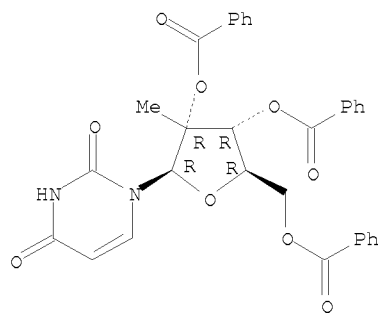
Absolute stereochemistry.



L11 ANSWER 7 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN  
 AN 2007:1164795 CAPLUS  
 DN 147:534049  
 TI 2'-C-methyl branched pyrimidine ribonucleoside analogues: potent inhibitors of RNA virus replication  
 AU Benzaria, Samira; Bardiot, Dorothee; Bouisset, Tony; Counor, Clement; Rabeson, Celine; Pierra, Claire; Storer, Richard; Loi, Anna Giulia; Cadeddu, Alessandra; Mura, Massimo; Musiu, Chiara; Liuzzi, Michel; Loddo, Roberta; Bergelson, Svetlana; Bichko, Vadim; Bridges, Edward; Cretton-Scott, Erika; Mao, John; Sommadossi, Jean-Pierre; Seifer, Maria; Standring, David; Tausek, Michele; Gosselin, Gilles; La Colla, Paolo  
 CS Laboratoire Cooperatif Idenix-CNRS-Universite Montpellier II, Montpellier, Fr.  
 SO Antiviral Chemistry & Chemotherapy (2007), 18(4), 225-242  
 CODEN: ACCHEH; ISSN: 0956-3202  
 PB International Medical Press, Ltd.  
 DT Journal  
 LA English  
 OS CASREACT 147:534049  
 AB RNA viruses are the agents of numerous wide-spread and often severe diseases. Their unique RNA-dependent RNA polymerase (RDRP) is essential for replication and, thus, constitutes a valid target for the development of selective chemotherapeutic agents. In this regard, the authors have investigated sugar-modified ribonucleoside analogs as potential inhibitors of the RDRP. Title compds. retain 'natural' pyrimidine bases, but possess a  $\beta$ -Me substituent at the 2'-position of the D- or L-ribose moiety. Evaluation against a broad range of RNA viruses, either single-stranded pos. (ssRNA+), single-stranded neg. (ssRNA-) or double-stranded (dsRNA), revealed potent activities for D-2'-C-methyl-cytidine and -uridine against ssRNA+, and dsRNA viruses. None of the L-enantiomers were active. Moreover, the 5'-triphosphates of the active D-enantiomers were found to inhibit the bovine virus diarrhea virus polymerase. Thus, the 2'-Me branching of natural pyrimidine ribonucleosides transforms physiol. mols. into potent, broad-spectrum antiviral agents that merit further development.  
 IT 23643-36-9P 957535-48-7P 957535-51-2P 957535-53-4P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (pyrimidine ribonucleoside analogs as potent inhibitors of RNA virus replication)  
 RN 23643-36-9 CAPLUS  
 CN 2,4(1H,3H)-Pyrimidinedione, 1-(2,3,5-tri-O-benzoyl-2-C-methyl- $\beta$ -D-ribofuranosyl)- (9CI) (CA INDEX NAME)

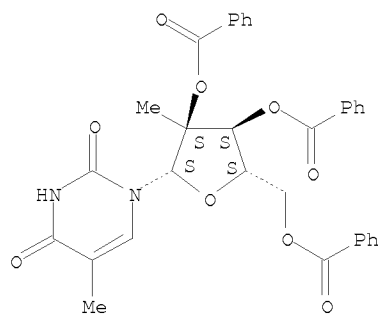
Absolute stereochemistry.

10/609,298



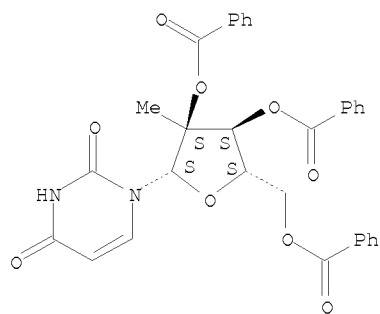
RN 957535-48-7 CAPLUS  
CN 2,4(1H,3H)-Pyrimidinedione, 5-methyl-1-(2,3,5-tri-O-benzoyl-2-C-methyl-β-L-ribofuranosyl)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 957535-51-2 CAPLUS  
CN 2,4(1H,3H)-Pyrimidinedione, 1-(2,3,5-tri-O-benzoyl-2-C-methyl-β-L-ribofuranosyl)- (CA INDEX NAME)

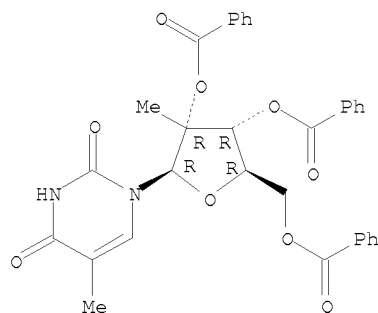
Absolute stereochemistry. Rotation (+).



RN 957535-53-4 CAPLUS  
CN Uridine, 5-methyl-2'-C-methyl-, 2',3',5'-tribenzoate (CA INDEX NAME)

Absolute stereochemistry.

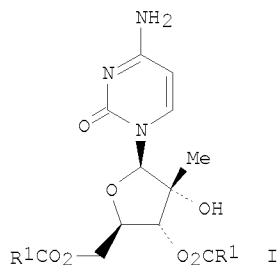
McIntosh



RE.CNT 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 8 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN  
AN 2007:1121524 CAPLUS  
DN 147:407046  
TI Preparation of nucleosides as Hepatitis C virus NS5b  
polymerase inhibitors and antiviral agents via regioselective O-acylation  
reaction  
IN Sarma, Keshab  
PA Roche Palo Alto LLC, USA  
SO U.S. Pat. Appl. Publ., 15pp.  
CODEN: USXXCO  
DT Patent  
LA English  
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20070232562	A1	20071004	US 2007-732983	20070404
WO 2007113159	A1	20071011	WO 2007-EP52866	20070326
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRAI US 2006-789491P	P	20060404		
OS CASREACT 147:407046; MARPAT 147:407046				
GI				



AB Nucleosides I, wherein R1 is Compds. having the formula I wherein R1 is C2-5 (un)-branched alkyl, C2-5 (un)-branched alkenyl, C3-5 cycloalkyl, C2-5 lower halo-alkyl, were prepared as Hepatitis C

virus NS5b polymerase inhibitors. Also disclosed are compns. and methods for inhibiting hepatitis replication, processes for making the compds. and synthetic intermediates used in the process. Thus, nucleoside I.HCl [R1 = C(O)Et] was prepared in 60% yield by regioselective O-acylation of I (R1 = H) with propionyl chloride. Title compds. were tested in vivo as Hepatitis C virus NS5b polymerase inhibitors and antiviral agents (a dose of between 1.0 and 6.0 g per day is administered to the patient). Determination of pharmacokinetic parameters of title nucleosides in rats, is reported.

IT 951131-56-9P 951131-58-1P 951131-60-5P

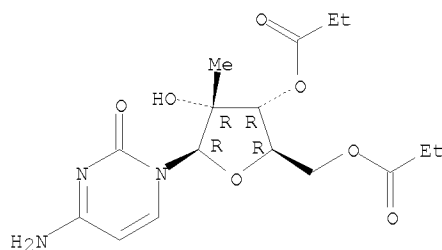
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of nucleosides as Hepatitis C virus NS5b polymerase inhibitors and antiviral agents via regioselective O-acylation reaction)

RN 951131-56-9 CAPLUS

CN Cytidine, 2'-C-methyl-, 3',5'-dipropanoate, hydrochloride (1:1) (CA INDEX NAME)

Absolute stereochemistry.

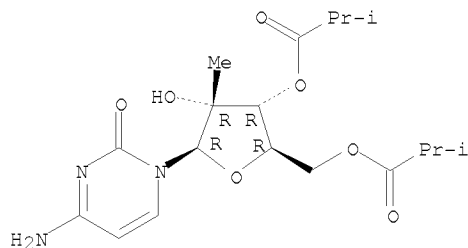


● HCl

RN 951131-58-1 CAPLUS

CN Cytidine, 2'-C-methyl-, 3',5'-bis(2-methylpropanoate), hydrochloride (1:1) (CA INDEX NAME)

Absolute stereochemistry.

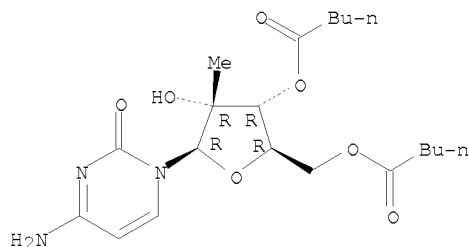


● HCl

RN 951131-60-5 CAPLUS

CN Cytidine, 2'-C-methyl-, 3',5'-dipentanoate, hydrochloride (1:1) (CA INDEX NAME)

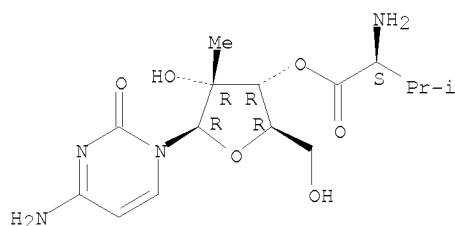
Absolute stereochemistry.



● HCl

IT 640281-90-9  
 RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU  
 (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (preparation of nucleosides as Hepatitis C virus NS5b  
 polymerase inhibitors and antiviral agents via regioselective  
 O-acylation reaction)  
 RN 640281-90-9 CAPLUS  
 CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L11 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN  
 AN 2007:1112011 CAPLUS  
 DN 147:514184  
 TI New therapies for hepatitis C  
 AU Modi, Apurva A.; Hoofnagle, Jay H.  
 CS Liver Diseases Branch, National Institute of Diabetes and Digestive and  
 Kidney Diseases, National Institutes of Health, Bethesda, MD, USA  
 SO Hepatology (Hoboken, NJ, United States) (2007), 46(3), 615-617  
 CODEN: HPTLD9; ISSN: 0270-9139  
 PB John Wiley & Sons, Inc.  
 DT Journal; General Review  
 LA English  
 AB A review. The research Forestier et al. (2007) entitled "Antiviral  
 activity of telaprevir (VX-950) and peginterferon alfa-2a in patients with  
 hepatitis C" is reviewed with commentary and refs.  
 Forestier and her coinvestigators from Saarland University Hospital, the  
 University of Amsterdam, and Vertex Pharmaceuticals describe the preliminary  
 clin. results of a small phase 1b trial of telaprevir. The report  
 provides information on HCV RNA and alanine aminotransferase  
 levels in 8 patients who received telaprevir alone, 8 who received  
 telaprevir with peginterferon, and 4 who served as controls and received  
 peginterferon alone for 2 wk. Telaprevir was then stopped, but the  
 patients were offered a continuation of treatment with a combination of  
 peginterferon and ribavirin until 48 wk and thus were provided the standard of  
 care for chronic hepatitis C, genotype 1. Telaprevir  
 led to a rapid decline in HCV RNA levels within 1-4 days. The  
 combination of peginterferon with telaprevir resulted in a similar early  
 decline in viral levels, but importantly, the combination therapy was  
 associated with an addnl., continuing decline after the first 4 days of  
 treatment.  
 IT 640281-90-9, Valopicitabine  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

10/609,298

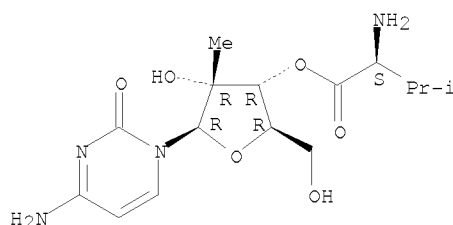
(Biological study); USES (Uses)

(valopicitabine, BILN-2061 showed greater toxicity hence were abandoned from usage by patient with hepatitis C)

RN 640281-90-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 10 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2007:1029651 CAPLUS

DN 147:365486

TI Preparation of 2-(phenylamino)thiazole derivatives as inhibitors of viral replication for the treatment of hepatitis C infection

IN Zhang, Suoming; Phadke, Avinash; Wang, Xiangzhu; Liu, Cuixian

PA Achillion Pharmaceuticals, Inc., USA

SO PCT Int. Appl., 134pp.

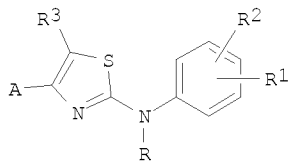
CODEN: PIXXD2

DT Patent

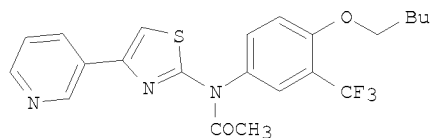
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2007103550	A2	20070913	WO 2007-US6023	20070308
	WO 2007103550	A3	20071108		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
	RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA			
	US 20070213301	A1	20070913	US 2007-683749	20070308
PRAI	US 2006-780609P	P	20060308		
OS	MARPAT 147:365486				
GI					



I



II

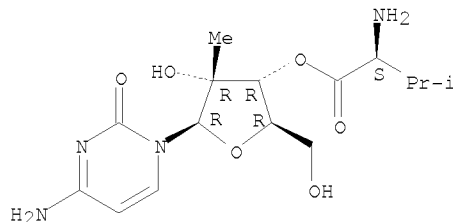
AB Title compds. I [wherein A = (un)substituted Ph, benzyl, heteroaryl, etc.; R = CHO, C(O)COOH, C(O)CONH<sub>2</sub>, etc.; R<sub>1</sub> = (un)substituted haloalkyl, haloalkoxy, alkylamino, etc.; R<sub>2</sub> (0-2 substituents) = halo, OH, amino, etc.; R<sub>3</sub> = H, halo, OH, etc.] and pharmaceutically acceptable salts thereof were prepared as inhibitors of viral replication. For instance, cyclocondensation of 3-bromoacetylpyridine with N-(4-pentoxymethyl-3-trifluoromethylphenyl)thiourea followed by acylation of the resultant anilinothiazole with acetyl chloride gave II. This product showed inhibition of HCV replication with an EC<sub>50</sub> of < 1 μM. Therefore, the invented compds. and their pharmaceutical compns. are useful for the treatment of hepatitis C infection.

IT 640281-90-9, Valopicitabine  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (co-drug; preparation of (phenylamino)thiazoles as inhibitors of viral replication for treatment of hepatitis C infection)

RN 640281-90-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L11 ANSWER 11 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2007:618644 CAPLUS

DN 147:31277

TI Polycyclic phenolic compounds and use in treating viral infections

IN Dugourd, Dominique

PA Migenix Corporation, Can.

SO PCT Int. Appl., 77pp.

CODEN: PIXXD2

DT Patent

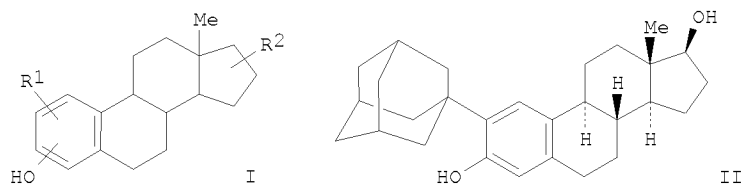
LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007062528	A1	20070607	WO 2006-CA1965	20061201
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,			

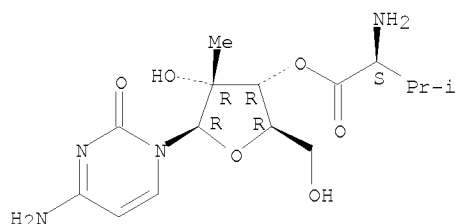


IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,  
 CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,  
 GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,  
 KG, KZ, MD, RU, TJ, TM  
 US 20070161611 A1 20070712 US 2006-565621 20061130  
 PRAI US 2005-742058P P 20051201  
 US 2006-565621 A 20061130  
 OS MARPAT 147:31277  
 GI



AB The present invention provides antiviral polycyclic phenolic compds.  
 (PPCs) of formula I [R1 = H, alkyl, aryl, cycloalkyl, etc.; R2 = H, OH,  
 acyl, oxo, = (substituted) NH, SH, etc.] for use in treating or preventing  
 viral infections and associated conditions, such as infections by  
 Flaviviridae, Hepadnaviridae, Herpesviridae, Papillomaviridae,  
 Retroviridae, Adenoviridae, or respiratory viruses (such as Adenoviridae,  
 Orthomyxoviridae, Paramyxoviridae and Coronaviridae). Thus, II was prepared  
 from estrone and 1-adamantanol, and inhibited viral release by 69% in  
 BVDV-infected MDBK cells.  
 IT 640281-90-9, Valopicitabine  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (co-drug; estrone derivs. for treatment of viral infections)  
 RN 640281-90-9 CAPLUS  
 CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 12 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN  
 AN 2007:412679 CAPLUS  
 DN 146:395250  
 TI Cyclosporin derivatives for the treatment and prevention of  
 hepatitis C infection  
 IN Houck, David Renwick  
 PA Scynexis, Inc., USA  
 SO PCT Int. Appl., 65pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007041632	A2	20070412	WO 2006-US38823	20061002
WO 2007041632	A3	20071213		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP,			

KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW  
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

AU 2006299426 A1 20070412 AU 2006-299426 20061002  
 US 20070173440 A1 20070726 US 2006-542930 20061002  
 PRAI US 2005-722679P P 20050930  
 US 2006-787549P P 20060329  
 WO 2006-US38823 W 20061002

OS MARPAT 146:395250

AB This invention relates to 3-ether or 3-thioether derivs. of cyclosporin or a pharmaceutically acceptable salt or solvate thereof, in combination with a second therapeutic agent for sequential or simultaneous administration in treatment and prevention of hepatitis C viral (HCV) infection. The second therapeutic agent is selected from modulators of NS3-4A protease, modulators of NS5B RNA-dependent RNA polymerase, and immunomodulatory agents. Thus, treatment of 1,4-diacetyl-3-methoxy-4-(gamma-hydroxymethylleucine)cyclosporin (275 mg) in methanol with 25 weight% sodium methoxide in methanol at room temperature yielded 33 mg of 3-methoxy-4-(gamma-hydroxymethylleucine)cyclosporin (Compound T). The Compound T potently inhibited HCV replication in human liver cells to a greater extent than cyclosporin used as a control. In addition, when considering the level of cytotoxicity, the compound exhibited a wider safety margin (for example, cytotoxicity IC50 vs. antiviral EC50) than cyclosporine. The combination of Compound T and interferon- $\alpha$  was additive.

IT 640281-90-9, Valopicitabine

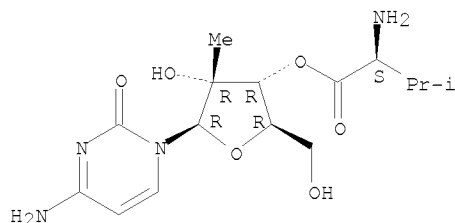
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(cyclosporin derivs. and their combinations for treatment and prevention of hepatitis C infection)

RN 640281-90-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L11 ANSWER 13 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2007:320324 CAPLUS

DN 146:394149

TI Valopicitabine dihydrochloride: a specific polymerase inhibitor of hepatitis C virus

AU Toniutto, Pierluigi; Fabris, Carlo; Bitetto, Davide; Fornasiere, Ezio; Rapetti, Rachele; Pirisi, Mario

CS Internal Medicine, Medical Liver Transplantation Unit, DPMSC, University of Udine, Udine, 33100, Italy

SO Current Opinion in Investigational Drugs (Thomson Scientific) (2007), 8(2), 150-158

CODEN: COIDAZ; ISSN: 1472-4472

PB Thomson Scientific

DT Journal; General Review

LA English

AB A review. Idenix Pharmaceuticals Inc and Novartis AG are codeveloping valopicitabine dihydrochloride, a once-daily oral nucleoside for the potential treatment of HCV infection. In Jan. 2005, a phase IIa clin. trial comparing valopicitabine dihydrochloride with pegylated IFN in

treatment-naïve HCV patients was ongoing, in addition to a phase IIb trial in patients that had previously failed pegylated IFN and ribavirin combination therapy. In Jan. 2006, an international phase III trial in treatment-refractory patients was planned for the first half of the year, with a phase III trial in treatment-naïve individuals planned for the second half of the year.

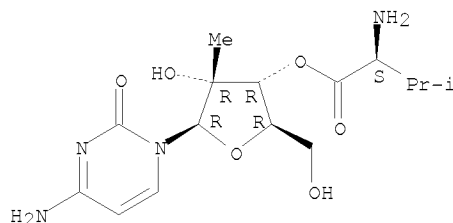
IT 640725-71-9, Valopicitabine dihydrochloride

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (valopicitabine dihydrochloride and interferon or ribavirin combination therapy was used to treat patient with hepatitis C virus infection)

RN 640725-71-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



● 2 HCl

RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 14 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2007:200728 CAPLUS

DN 146:274570

TI Preparation of 2'-C-Me nucleoside 5'-monophosphate and 4'-C-Me nucleoside 5'-monophosphate prodrugs for the treatment of hepatitis C viral infection

IN Erion, Mark D.; Reddy, K. Raja; Maccoss, Malcolm; Olsen, David B.

PA Merck & Co., Inc., USA; Metabasis Therapeutics, Inc.

SO PCT Int. Appl., 268pp.

CODEN: PIXXD2

DT Patent

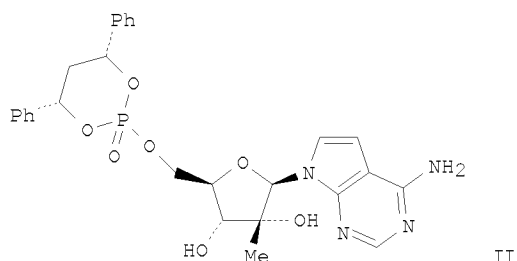
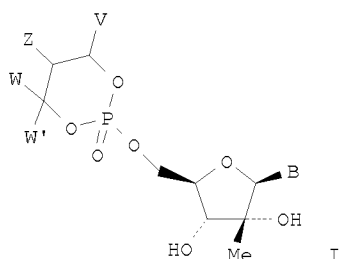
LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007022073	A2	20070222	WO 2006-US31614	20060814
WO 2007022073	A3	20071115		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA			
AU 2006279720	A1	20070222	AU 2006-279720	20060814
CA 2618713	A1	20070222	CA 2006-2618713	20060814
EP 1915053	A2	20080430	EP 2006-801410	20060814
R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS			
PRAI US 2005-707767P	P	20050812		

10/609,298

US 2006-772649P P 20060213  
WO 2006-US31614 W 20060814  
OS MARPAT 146:274570  
GI



AB 2'-C-Me nucleoside 5'-monophosphate and 4'-C-Me nucleoside 5'-monophosphate prodrugs I, wherein B can be heterocyclic or heteroaryl rings; V is an optionally substituted monocyclic aryl or heteroaryl ring; W and W' are independently (un)substituted monocyclic aryl or heteroaryl rings, alkyl, aryl, heterocycloaryl or aralkyl groups; Z is halo, cyano, keto, amido, etc. are prepared Further, I can also be prepared such that V and Z are connected via 3-5 atoms to form a cyclic group fused to aryl groups; Z and W connected via 3-5 atoms to form a cyclic group containing one heteroarom; or W and W' connected via an addnl. 2-5 atoms to form a cyclic group optionally containing 0-2 heteroatoms. Thus, II was prepared and tested for its in vitro activation in human liver microsomes by product capture (0.044 nmol/mg/min at activation 250  $\mu$ M). I were also tested for their NTP accumulation in hepatocytes; in HCV-infected human liver assays; for tissue distribution following oral administration and the oral bioavailability in normal male rats.

IT 926655-64-3P 926655-66-5P 926655-67-6P  
926655-68-7P 926655-69-8P 926655-73-4P  
926655-74-5P 926655-75-6P 926655-76-7P  
926655-77-8P 926655-78-9P 926655-80-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 2'-C-Me nucleoside 5'-monophosphate and 4'-C-Me nucleoside 5'- monophosphate prodrugs for the treatment of hepatitis C viral infection)

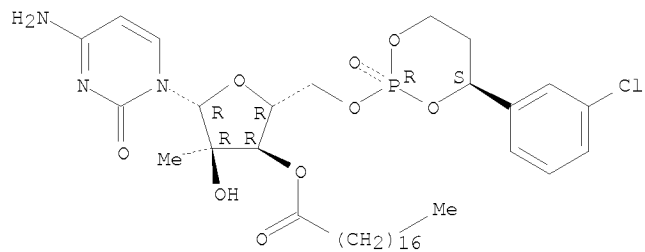
RN 926655-64-3 CAPLUS

CN Cytidine, 5'-O-[(2R,4S)-4-(3-chlorophenyl)-2-oxido-1,3,2-dioxaphosphorinan-2-yl]-2'-C-methyl-, 3'-octadecanoate (CA INDEX NAME)

Absolute stereochemistry.

McIntosh

10/609,298



RN 926655-66-5 CAPLUS

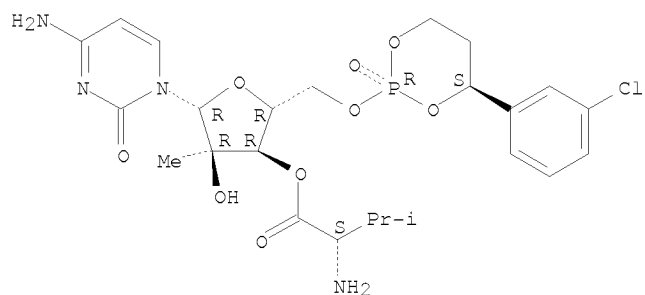
CN L-Valine, 3'-ester with 5'-O-[(2R,4S)-4-(3-chlorophenyl)-2-oxido-1,3,2-dioxaphosphorinan-2-yl]-2'-C-methylcytidine, 2,2,2-trifluoroacetate (1:?)  
(CA INDEX NAME)

CM 1

CRN 926655-65-4

CMF C24 H32 Cl N4 O9 P

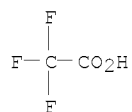
Absolute stereochemistry.



CM 2

CRN 76-05-1

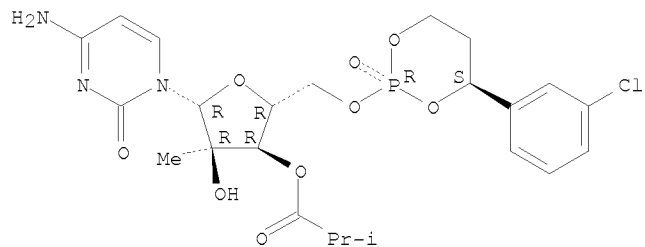
CMF C2 H F3 O2



RN 926655-67-6 CAPLUS

CN Cytidine, 5'-O-[(2R,4S)-4-(3-chlorophenyl)-2-oxido-1,3,2-dioxaphosphorinan-2-yl]-2'-C-methyl-, 3'-(2-methylpropanoate) (CA INDEX NAME)

Absolute stereochemistry.

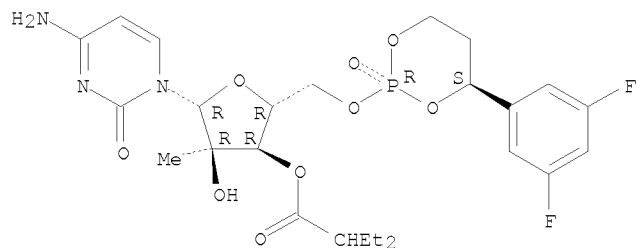


McIntosh

10/609,298

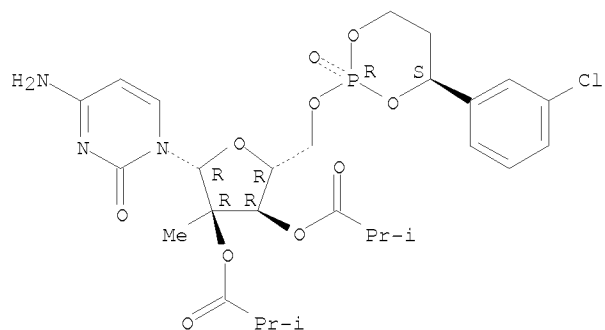
RN 926655-68-7 CAPLUS  
CN Cytidine, 5'-O-[(2R,4S)-4-(3,5-difluorophenyl)-2-oxido-1,3,2-dioxaphosphorinan-2-yl]-2'-C-methyl-, 3'-(2-ethylbutanoate) (CA INDEX NAME)

Absolute stereochemistry.



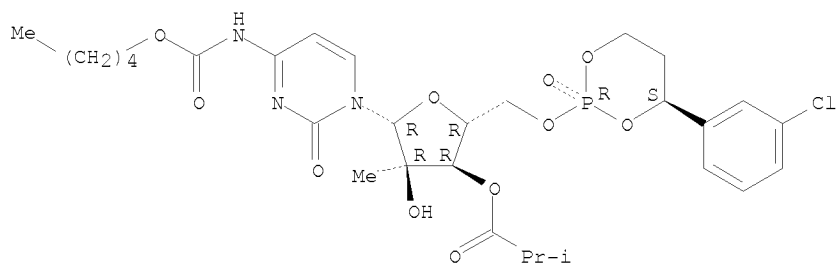
RN 926655-69-8 CAPLUS  
CN Cytidine, 5'-O-[(2R,4S)-4-(3-chlorophenyl)-2-oxido-1,3,2-dioxaphosphorinan-2-yl]-2'-C-methyl-, 2',3'-bis(2-methylpropanoate) (CA INDEX NAME)

Absolute stereochemistry.



RN 926655-73-4 CAPLUS  
CN Cytidine, 5'-O-[(2R,4S)-4-(3-chlorophenyl)-2-oxido-1,3,2-dioxaphosphorinan-2-yl]-2'-C-methyl-N-[(pentyloxy)carbonyl]-, 3'-(2-methylpropanoate) (CA INDEX NAME)

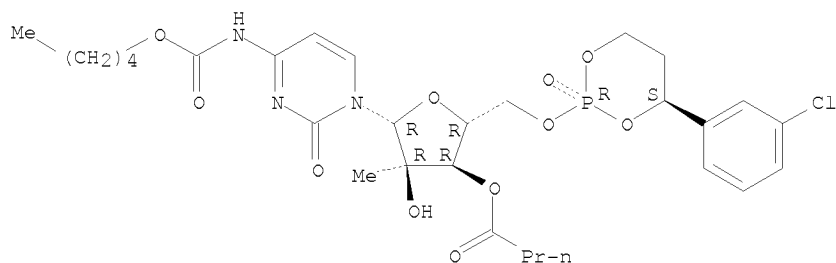
Absolute stereochemistry.



RN 926655-74-5 CAPLUS  
CN Cytidine, 5'-O-[(2R,4S)-4-(3-chlorophenyl)-2-oxido-1,3,2-dioxaphosphorinan-2-yl]-2'-C-methyl-N-[(pentyloxy)carbonyl]-, 3'-butanoate (CA INDEX NAME)

Absolute stereochemistry.

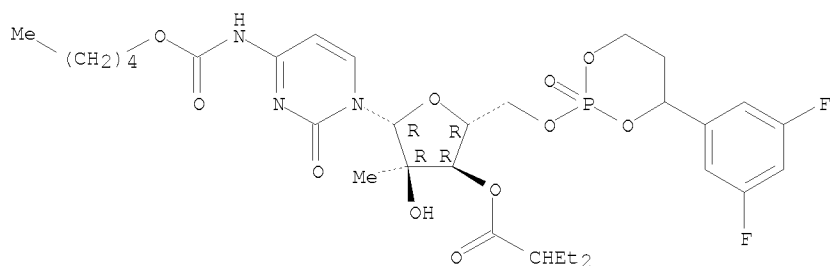
10/609,298



RN 926655-75-6 CAPLUS

CN Cytidine, 5'-O-[4-(3,5-difluorophenyl)-2-oxido-1,3,2-dioxaphosphorinan-2-yl]-2'-C-methyl-N-[(pentyloxy)carbonyl]-, 3'-(2-ethylbutanoate) (CA INDEX NAME)

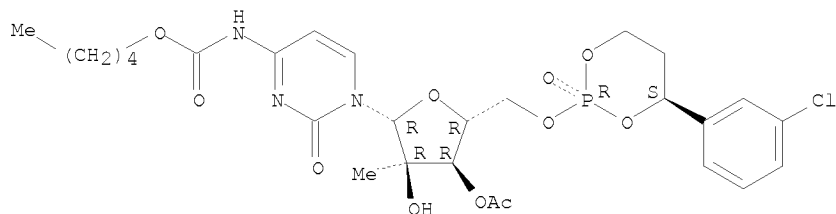
Absolute stereochemistry.



RN 926655-76-7 CAPLUS

CN Cytidine, 5'-O-[(2R,4S)-4-(3-chlorophenyl)-2-oxido-1,3,2-dioxaphosphorinan-2-yl]-2'-C-methyl-N-[(pentyloxy)carbonyl]-, 3'-acetate (CA INDEX NAME)

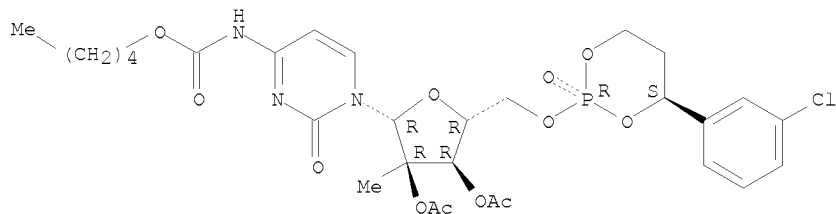
Absolute stereochemistry.



RN 926655-77-8 CAPLUS

CN Cytidine, 5'-O-[(2R,4S)-4-(3-chlorophenyl)-2-oxido-1,3,2-dioxaphosphorinan-2-yl]-2'-C-methyl-N-[(pentyloxy)carbonyl]-, 2',3'-diacetate (CA INDEX NAME)

Absolute stereochemistry.



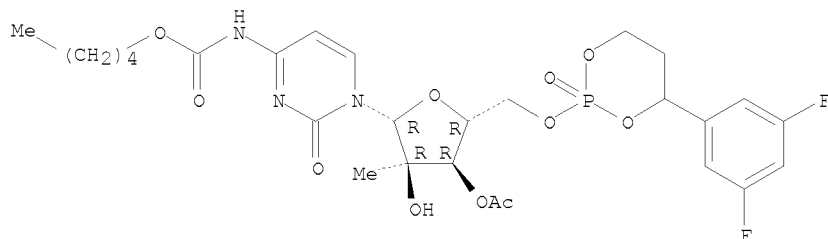
RN 926655-78-9 CAPLUS

CN Cytidine, 5'-O-[4-(3,5-difluorophenyl)-2-oxido-1,3,2-dioxaphosphorinan-2-yl]-2'-C-methyl-N-[(pentyloxy)carbonyl]-, 3'-acetate (CA INDEX NAME)

McIntosh

10/609,298

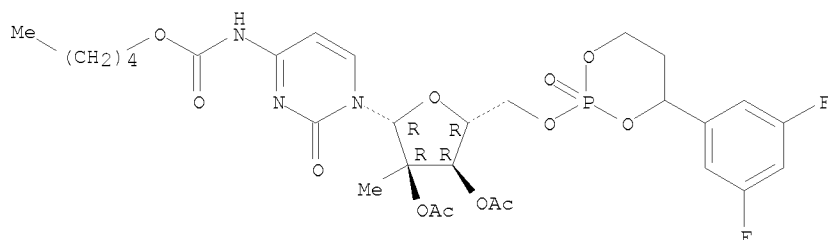
Absolute stereochemistry.



RN 926655-80-3 CAPLUS

CN Cytidine, 5'-O-[4-(3,5-difluorophenyl)-2-oxido-1,3,2-dioxaphosphorinan-2-yl]-2'-C-methyl-N-[(pentyloxy)carbonyl]-, 2',3'-diacetate (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 15 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2007:85871 CAPLUS

DN 146:177157

TI Small animal model for HCV replication

IN Weiner, Amy; Aukerman, Sharon Lea; Mendel, Dirk; Zhu, Qing

PA Novartis A.-G., Switz.

SO PCT Int. Appl., 85pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2007011777	A2	20070125	WO 2006-US27485	20060715
	WO 2007011777	A3	20071011		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
CA	2615626	A1	20070125	CA 2006-2615626	20060715
EP	1909564	A2	20080416	EP 2006-787397	20060715
R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS				
PRAI	US 2005-700475P	P	20050718		
	US 2006-776640P	P	20060223		
	WO 2006-US27485	W	20060715		
AB	An animal model for HCV (hepatitis C virus) replication and/or production of virus or virus like particles is provided. The invention utilizes an HCV replicon present in a cell to				

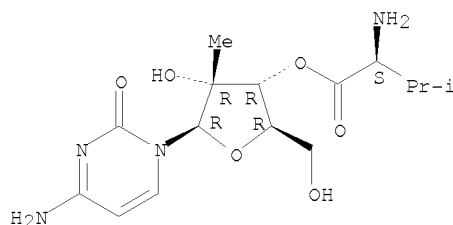
McIntosh



deliver HCV nucleic acid and replicate and express HCV proteins in an animal model comprising an animal that has been immunocompromised. The invention further provides a method of treatment or prevention of HCV in a mammal which comprises administering to the mammal a combination which comprises an immunomodulatory compound and another antiviral agent. Also provided are cell lines showing a decreased sensitivity to interferon alpha or some other immunomodulator and methods of making or isolating such cell lines.

IT 640281-90-9, Valopicitabine  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (small animal model for hepatitis C virus replication)  
 RN 640281-90-9 CAPLUS  
 CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L11 ANSWER 16 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN  
 AN 2006:1283521 CAPLUS  
 DN 146:20343  
 TI Use of 4-[3,5-Bis-(2-hydroxyphenyl)-[1,2,4]-triazol-1-yl]benzoic acid for the treatment of liver diseases in which iron plays a role in pathogenesis  
 IN Alberti, Daniele; Marks, Peter; Nick, Hanspeter; Rojckjaer, Lisa Grace  
 PA Novartis AG, Switz.; Novartis Pharma GmbH  
 SO PCT Int. Appl., 20pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006130532	A2	20061207	WO 2006-US20677	20060530
WO 2006130532	A3	20071122		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA			
AU 2006252718	A1	20061207	AU 2006-252718	20060530
CA 2608709	A1	20061207	CA 2006-2608709	20060530
EP 1893198	A2	20080305	EP 2006-771445	20060530
R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU			
CN 101180053	A	20080514	CN 2006-80017617	20071121
KR 2008003933	A	20080108	KR 2007-727922	20071129
MX 200715085	A	20080117	MX 2007-15085	20071129
NO 2007006595	A	20071220	NO 2007-6595	20071220
PRAI US 2005-685848P	P	20050531		
US 2005-692808P	P	20050622		
US 2006-746786P	P	20060509		
WO 2006-US20677	W	20060530		

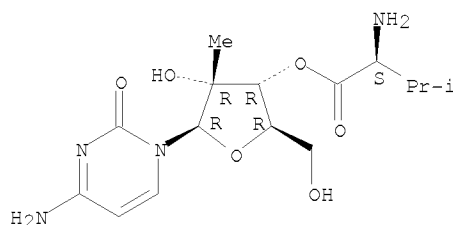
AB The invention discloses use of 4-[3,5-Bis-(2-hydroxyphenyl)-[1,2,4]-triazol-1-yl]benzoic acid for the manufacture of pharmaceutical compns. for the treatment of liver diseases in humans in which iron plays a role in pathogenesis, including viral diseases, e.g. chronic hepatitis C, optionally in conjunction with antiviral agents and for the treatment of nonviral diseases, e.g. non-alc. steatohepatitis and non-alc. fatty liver disease.

IT 640281-90-9, Valopicitabine  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (triazolyl benzoic acid derivative for treatment of liver diseases in which iron plays role in pathogenesis)

RN 640281-90-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L11 ANSWER 17 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2006:1257296 CAPLUS

DN 146:54578

TI Recent patents on nucleoside and nucleotide inhibitors for HCV

AU Shim, Jae H.; Hong, Zhi; Wu, Jim Z.

CS Drug Discovery, Valeant Pharmaceuticals International, Costa Mesa, CA, 92626, USA

SO Recent Patents on Anti-Infective Drug Discovery (2006), 1(3), 323-331  
 CODEN: RPADCX; ISSN: 1574-891X

PB Bentham Science Publishers Ltd.

DT Journal; General Review

LA English

AB A review. Hepatitis C virus (HCV) infection is a leading cause of liver diseases such as cirrhosis and hepatocellular carcinoma. There are estimated 170 million people worldwide chronically infected with the virus. The lack of highly effective and safe therapeutics for HCV infection has spurred intensive efforts to develop anti-HCV drugs as evidenced by the large number of new patent applications filed each year. Nucleoside and nucleotide inhibitors are the analogs of DNA or RNA substrates, and they inhibit viral polymerases by acting as chain terminators, viral mutagens, or simple competitive inhibitors. The successful development of various nucleoside and nucleotide inhibitors for the treatment of HIV and HBV infections has prompted the drug industry to seek similar strategies for HCV. This review summarizes recently issued or published patents covering nucleoside and nucleotide inhibitors for HCV. The claimed chemical structures and available biol. activities, mechanism of action, and drug resistance profiles are discussed. The development status of several promising nucleoside inhibitors is also described.

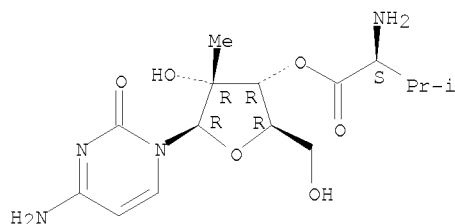
IT 640725-71-9, NM283  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (recent patents on nucleoside and nucleotide inhibitors for HCV)

RN 640725-71-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

10/609,298

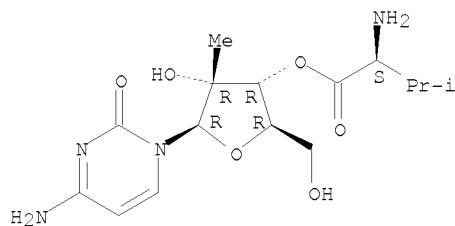


● 2 HCl

RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 18 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN  
AN 2006:1086375 CAPLUS  
DN 146:54739  
TI Ribavirin antagonizes the in vitro anti-hepatitis C virus activity of 2'-C-methylcytidine, the active component of valopicitabine  
AU Coelmont, Lotte; Paeshuyse, Jan; Windisch, Marc P.; De Clercq, Erik; Bartenschlager, Ralf; Neyts, Johan  
CS Rega Institute for Medical Research, KULeuven, Louvain, 3000, Belg.  
SO Antimicrobial Agents and Chemotherapy (2006), 50(10), 3444-3446  
CODEN: AMACQ; ISSN: 0066-4804  
PB American Society for Microbiology  
DT Journal  
LA English  
AB Ribavirin antagonizes the in vitro anti-hepatitis C virus (HCV) activity of the pyrimidine nucleoside analog 2'-C-methylcytidine, the active component of the exptl. anti-HCV drug valopicitabine. In contrast, the combination of ribavirin with either the purine nucleoside analog 2'-C-methyladenosine or the HCV protease inhibitor VX-950 resulted in an additive antiviral activity. These findings may have implications when planning clin. studies with valopicitabine.  
IT 640281-90-9D, Valopicitabine, metabolite  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(ribavirin antagonizes anti-hepatitis C virus activity of 2'-C-methylcytidine, active component of valopicitabine)  
RN 640281-90-9 CAPLUS  
CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



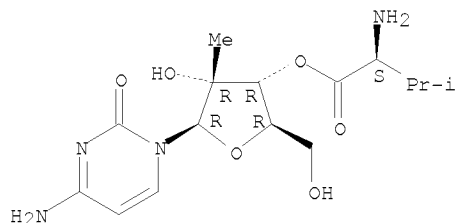
RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 19 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN  
AN 2006:1045856 CAPLUS  
DN 146:28022  
TI Synthesis and Pharmacokinetics of Valopicitabine (NM283), an Efficient Prodrug of the Potent Anti-HCV Agent 2'-C-Methylcytidine  
AU Pierra, Claire; Amador, Agnes; Benzaria, Samira; Cretton-Scott, Erika; D'Amours, Marc; Mao, John; Mathieu, Steven; Moussa, Adel; Bridges, Edward

McIntosh

G.; Standing, David N.; Sommadossi, Jean-Pierre; Storer, Richard; Gosselin, Gilles  
 CS Laboratoire Cooperatif Idenix-CNRS-Universite Montpellier II Case Courrier  
 008, Universite Montpellier II, Montpellier, 34095, Fr.  
 SO Journal of Medicinal Chemistry (2006), 49(22), 6614-6620  
 CODEN: JMCMAR; ISSN: 0022-2623  
 PB American Chemical Society  
 DT Journal  
 LA English  
 OS CASREACT 146:28022  
 AB In the search for new therapeutic agents against chronic hepatitis C, 2'-C-methylcytidine was discovered to be a potent and selective inhibitor in cell culture of a number of RNA viruses, including the pestivirus bovine viral diarrhea virus, a surrogate model for hepatitis C virus (HCV), and three flaviviruses, namely, yellow fever virus, West Nile virus, and dengue-2 virus. However, pharmacokinetic studies revealed that 2'-C-methylcytidine suffers from a low oral bioavailability. To overcome this limitation, the authors have synthesized the 3'-O-L-valinyl ester derivative (NM-283; dihydrochloride salt of valopicitabine) of 2'-C-methylcytidine. The authors present the chemical synthesis and physicochem. characteristics of NM-283, anti-HCV prodrug candidate, as well as a comparative study of its pharmacokinetic parameters with those of its parent nucleoside analog, 2'-C-methylcytidine.  
 IT 640725-71-9P  
 RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
 (preparation and pharmacokinetics of NM-283, a prodrug of anti-HCV agent 2'-C-methylcytidine)  
 RN 640725-71-9 CAPLUS  
 CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA INDEX NAME)

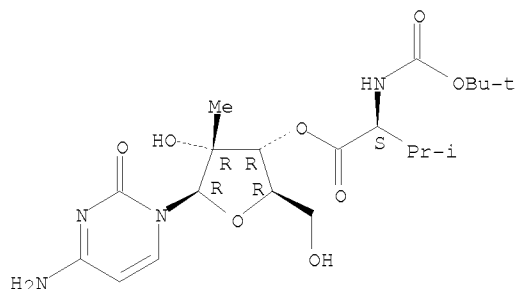
Absolute stereochemistry. Rotation (+).



● 2 HCl

IT 640725-70-8P 642075-44-3P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and pharmacokinetics of NM-283, a prodrug of anti-HCV agent 2'-C-methylcytidine)  
 RN 640725-70-8 CAPLUS  
 CN L-Valine, N-[(1,1-dimethylethoxy)carbonyl]-, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry.

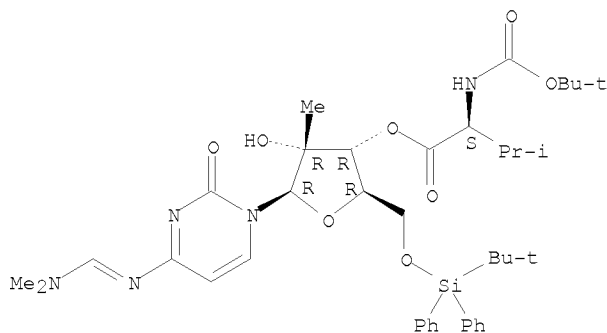


RN 642075-44-3 CAPLUS

CN L-Valine, N-[(1,1-dimethylethoxy)carbonyl]-, 3'-ester with  
 5'-O-[(1,1-dimethylethyl)diphenylsilyl]-N-[(dimethylamino)methylene]-2'-C-  
 methylcytidine (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.



RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 20 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2006:945608 CAPLUS

DN 145:315225

TI Bicyclic nucleosides and nucleotides as therapeutic agents

IN Francom, Paula; Nearn, Roland Henry; Draffan, Alistair George; Lambert,  
 John Nicholas; Bond, Silas

PA Biota, Inc., USA

SO PCT Int. Appl., 107pp.

CODEN: PIXXD2

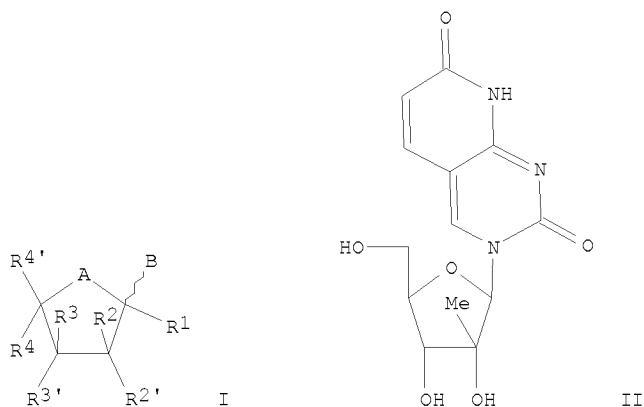
DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006094347	A1	20060914	WO 2006-AU303	20060308
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2006222563	A1	20060914	AU 2006-222563	20060308
CA 2600886	A1	20060914	CA 2006-2600886	20060308
EP 1858889	A1	20071128	EP 2006-704976	20060308

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,  
 IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR  
 PRAI US 2005-661665P P 20050308  
 WO 2006-AU303 W 20060308  
 OS CASREACT 145:315225  
 GI



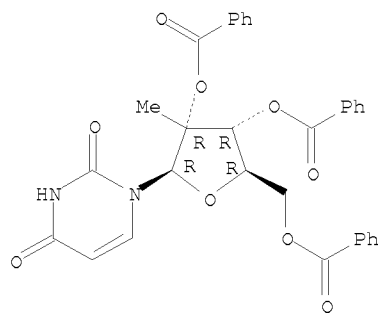
AB The invention relates to the use of bicyclic nucleosides and nucleotides I, wherein: A is O, S, CH<sub>2</sub>, CHF, CF<sub>2</sub> or NR; B is bicyclic heterocycle; R<sub>1</sub>, R<sub>2</sub>, R<sub>2</sub>', R<sub>3</sub>, R<sub>3</sub>', and R<sub>4</sub> are independently H, halogen, OH, N<sub>3</sub>, CN, alkyl, alkenyl, alkynyl, aryl, acyl, arylalkyl, heterocyclyl, heteroaryl, cycloalkyl, cycloalkenyl, alkyloxy, alkenyloxy, alkynoxy, aryloxy, acyloxy, oxyacyl, arylalkoxy, heterocycloxy, heteroaryloxy, cycloalkoxy, cycloalkenoxy, amino, aminoacyl, aminoacyloxy, acylamino, oxyacylamino, oxyacyloxy, acylimino, acyliminoxy, oxyacylimino, aminothioacyl, thioacylamino, aminosulfinyl, aminosulfonyl, thio, thioacyl, thioacyloxy, oxythioacyl, oxythioacyloxy, optionally; R<sub>2</sub> and R<sub>2</sub>' together or R<sub>3</sub> and R<sub>3</sub>' together represents =O, =S, or =L-Y' where L is N, CH, CF, CCl or CBr and Y' is H, halogen, N<sub>3</sub>, Me, Et or CN; R<sub>4</sub>' is -CY<sub>2</sub>SH, -CY<sub>2</sub>OH, -CY<sub>2</sub>NH, or L'-R<sub>5</sub>; L' is selected from the group consisting of -CY<sub>2</sub>-, -CY<sub>2</sub>CY<sub>2</sub>-, -CY<sub>2</sub>OCY<sub>2</sub>-, -CY<sub>2</sub>SCY<sub>2</sub>- and -CY<sub>2</sub>NHCY<sub>2</sub>-; Y is H, OR, halogen, alkyl, alkenyl, alkynyl; R<sub>5</sub> is OR, NR<sub>2</sub>, monophosphate, diphosphate, and triphosphate, or a mono, di or triphosphate mimic; each R is independently H, CF<sub>3</sub>, alkyl, alkenyl, alkynyl, aryl, acyl, cycloalkyl, cycloalkenyl, heteroaryl, heterocyclyl; were prepared for the treatment of infectious diseases, and in particular, viral infections. Title compds. were typically active in the replicon assay in the range 1 to >1000 μM and cytotoxic in the range 30 to >100 μM. HCV-polymerase inhibition by title compds. is also reported.

IT 23643-36-9P 909394-67-8P 909394-72-5P  
 909394-73-6P 909394-74-7P 909394-75-8P  
 909394-76-9P 909394-77-0P 909394-81-6P  
 909394-82-7P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of bicyclic nucleosides and nucleotides as therapeutic agents)

RN 23643-36-9 CAPLUS  
 CN 2,4(1H,3H)-Pyrimidinedione, 1-(2,3,5-tri-O-benzoyl-2-C-methyl-β-D-ribofuranosyl)- (9CI) (CA INDEX NAME)

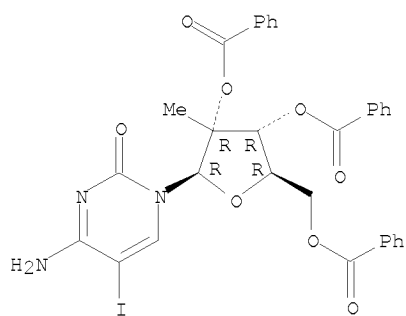
Absolute stereochemistry.

10/609,298



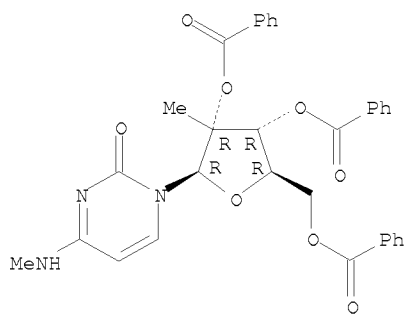
RN 909394-67-8 CAPLUS  
CN Cytidine, 5-iodo-2'-C-methyl-, 2',3',5'-tribenzoate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 909394-72-5 CAPLUS  
CN Cytidine, N-methyl-2'-C-methyl-, 2',3',5'-tribenzoate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

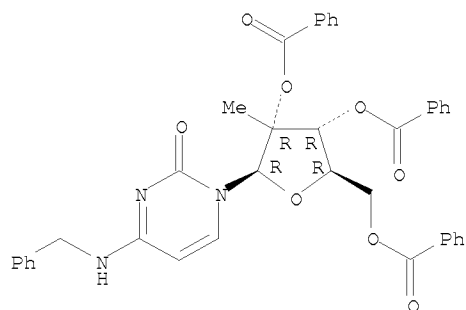


RN 909394-73-6 CAPLUS  
CN Cytidine, 2'-C-methyl-N-(phenylmethyl)-, 2',3',5'-tribenzoate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

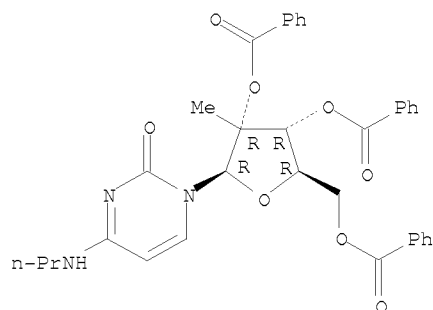
McIntosh

10/609,298



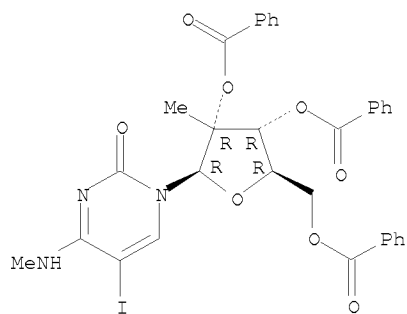
RN 909394-74-7 CAPLUS  
CN Cytidine, 2'-C-methyl-N-propyl-, 2',3',5'-tribenzoate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 909394-75-8 CAPLUS  
CN Cytidine, 5-iodo-N-methyl-2'-C-methyl-, 2',3',5'-tribenzoate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



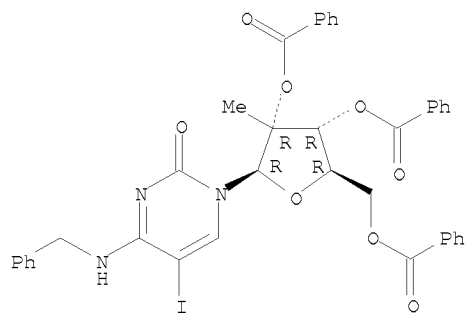
RN 909394-76-9 CAPLUS  
CN Cytidine, 5-iodo-2'-C-methyl-N-(phenylmethyl)-, 2',3',5'-tribenzoate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

McIntosh

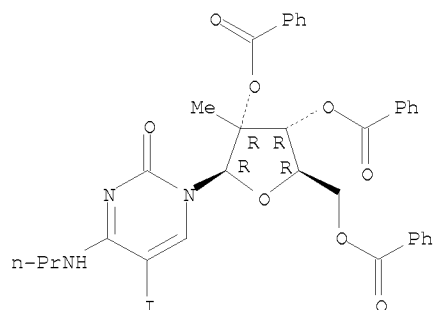


10/609,298



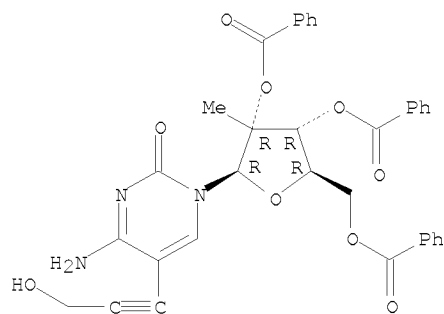
RN 909394-77-0 CAPLUS  
CN Cytidine, 5-iodo-2'-C-methyl-N-propyl-, 2',3',5'-tribenzoate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 909394-81-6 CAPLUS  
CN Cytidine, 5-(3-hydroxy-1-propynyl)-2'-C-methyl-, 2',3',5'-tribenzoate (9CI) (CA INDEX NAME)

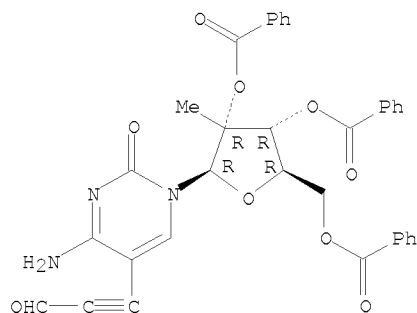
Absolute stereochemistry.



RN 909394-82-7 CAPLUS  
CN Cytidine, 2'-C-methyl-5-(3-oxo-1-propynyl)-, 2',3',5'-tribenzoate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

McIntosh



RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 21 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2006:894484 CAPLUS

DN 145:285094

TI Glucosidase inhibitor combinations with adjunctive therapies for treating  
or preventing Flaviviridae infections

IN Dugourd, Dominique; Rubinchik, Evelina; Clement, Jacob; Friedland, Hillel  
David

PA Migenix Inc., Can.

SO U.S. Pat. Appl. Publ., 69pp.

CODEN: USXXCO

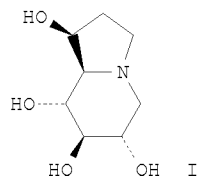
DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 20060194835	A1	20060831	US 2006-351885	20060209
	AU 2006221080	A1	20060914	AU 2006-221080	20060209
	CA 2597213	A1	20060914	CA 2006-2597213	20060209
	WO 2006096285	A2	20060914	WO 2006-US4927	20060209
	WO 2006096285	A3	20070125		
	W:				
	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW:				
	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	EP 1853317	A2	20071114	EP 2006-748202	20060209
	R:				
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	MX 200709561	A	20080114	MX 2007-9561	20070808
	IN 2007KN03225	A	20080321	IN 2007-KN3225	20070831
	KR 2007102741	A	20071019	KR 2007-720540	20070907
PRAI	US 2005-651910P	P	20050209		
	US 2005-664297P	P	20050321		
	US 2005-735464P	P	20051112		
	WO 2006-US4927	W	20060209		

GI



AB The present disclosure relates generally to compns. having a glucosidase inhibitor [castanospermine (I) or a derivative thereof, such as celgosivir] in combination with adjunctive therapies of compds. that alter immune function (such as interferon) and compds. that alter viral replication (such as nucleoside analogs like ribavirin), which can be used to treat or prevent infections caused by or associated with a virus of the Flaviviridae family, particularly infections caused by or associated with Hepatitis C virus (HCV). Examples include synergy of castanospermine or celgosivir in combination with other drugs such as interferons in a checkboard approach.

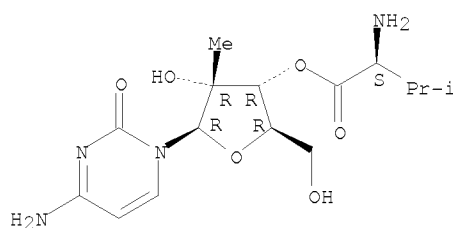
IT 640725-71-9, NM283

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(glucosidase inhibitor combinations with adjunctive therapies for treating or preventing Flaviviridae infections)

RN 640725-71-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



● 2 HCl

L11 ANSWER 22 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2006:774481 CAPLUS

DN 146:402230

TI Synthesis of 2'-C-methylcytidine and 2'-C-methyluridine derivatives modified in the 3'-position as potential antiviral agents

AU Pierra, Claire; Amador, Agnes; Badaroux, Eric; Storer, Richard; Gosselin, Gilles

CS Laboratoire Cooperatif Idenix-CNRS-Universite Montpellier II, Universite Montpellier II, Montpellier, 34095/5, Fr.

SO Collection of Czechoslovak Chemical Communications (2006), 71(7), 991-1010 CODEN: CCCCAK; ISSN: 0010-0765

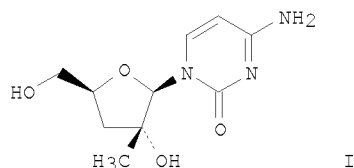
PB Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic

DT Journal

LA English

OS CASREACT 146:402230

GI

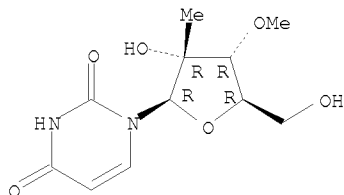


AB 2'-C-methylcytidine and 2'-C-methyluridine derivs. modified in the 3'-position, e.g. I·HCl, were prepared via Barton deoxygenation, amination, stereoselective cyclization, ring opening and fluorination from 2'-C-methyluridine or uridine. The antiviral activity of the title compds. was tested against RNA viruses and was found to be inactive. It was found that the modification at the 3'-position resulted in loss of

10/609,298

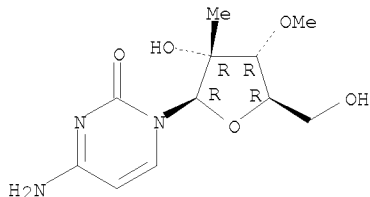
antiviral activity.  
IT 934014-31-0P  
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)  
(no activity; preparation and antiviral activity of methylcytidine and methyluridine derivs. via Barton deoxygenation, amination, stereoselective cyclization, ring opening and fluorination from methyluridine or uridine)  
RN 934014-31-0 CAPLUS  
CN Uridine, 2'-C-methyl-3'-O-methyl- (CA INDEX NAME)

Absolute stereochemistry.



IT 934014-32-1P  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(no activity; preparation and antiviral activity of methylcytidine and methyluridine derivs. via Barton deoxygenation, amination, stereoselective cyclization, ring opening and fluorination from methyluridine or uridine)  
RN 934014-32-1 CAPLUS  
CN Cytidine, 2'-C-methyl-3'-O-methyl-, hydrochloride (1:1) (CA INDEX NAME)

Absolute stereochemistry.



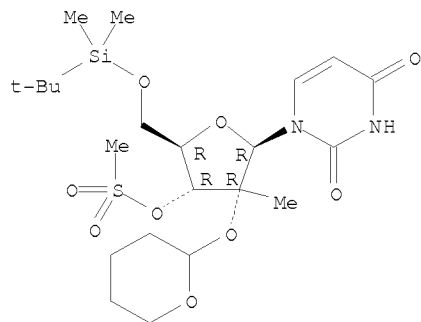
● HCl

IT 934014-23-0P 934014-24-1P 934014-27-4P  
934014-28-5P 934014-30-9P 934014-42-3P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and antiviral activity of methylcytidine and methyluridine derivs. via Barton deoxygenation, amination, stereoselective cyclization, ring opening and fluorination from methyluridine or uridine)  
RN 934014-23-0 CAPLUS  
CN Uridine, 5'-O-[(1,1-dimethylethyl)dimethylsilyl]-2'-C-methyl-2'-O-(tetrahydro-2H-pyran-2-yl)-, 3'-methanesulfonate (CA INDEX NAME)

Absolute stereochemistry.

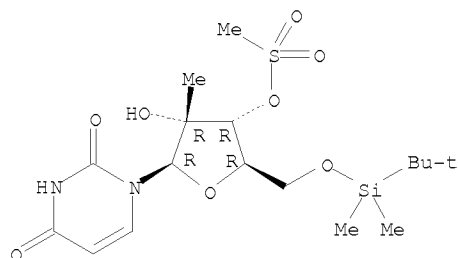
McIntosh

10/609,298



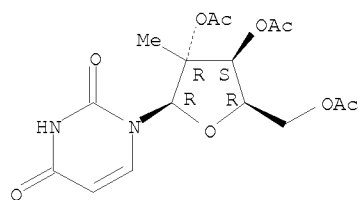
RN 934014-24-1 CAPLUS  
CN Uridine, 5'-O-[(1,1-dimethylethyl)dimethylsilyl]-2'-C-methyl-,  
3'-methanesulfonate (CA INDEX NAME)

Absolute stereochemistry.



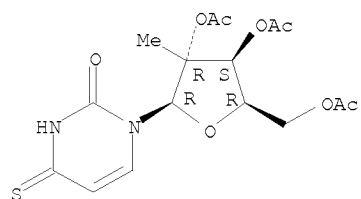
RN 934014-27-4 CAPLUS  
CN 2,4(1H,3H)-Pyrimidinedione, 1-(2,3,5-tri-O-acetyl-2-C-methyl- $\beta$ -D-  
xylofuranosyl)- (CA INDEX NAME)

Absolute stereochemistry.



RN 934014-28-5 CAPLUS  
CN 2(1H)-Pyrimidinone, 3,4-dihydro-4-thioxo-1-(2,3,5-tri-O-acetyl-2-C-methyl-  
 $\beta$ -D-xylofuranosyl)- (CA INDEX NAME)

Absolute stereochemistry.

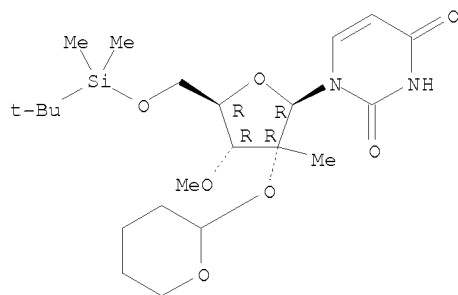


RN 934014-30-9 CAPLUS  
CN Uridine, 5'-O-[(1,1-dimethylethyl)dimethylsilyl]-2'-C-methyl-3'-O-methyl-  
2'-O-(tetrahydro-2H-pyran-2-yl)- (CA INDEX NAME)

McIntosh

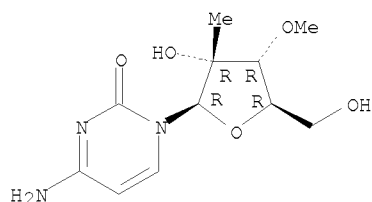
10/609,298

Absolute stereochemistry.



RN 934014-42-3 CAPLUS  
CN Cytidine, 2'-C-methyl-3'-O-methyl- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 23 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN  
AN 2006:708636 CAPLUS  
DN 146:19039  
TI Valopicitabine: anti-hepatitis C virus drug  
RNA-directed RNA polymerase (NS5B) inhibitor  
AU Sorbera, L. A.; Castaner, J.; Leeson, P. A.  
CS Prous Science, Barcelona, 08080, Spain  
SO Drugs of the Future (2006), 31(4), 320-324  
CODEN: DRFUD4; ISSN: 0377-8282  
PB Prous Science  
DT Journal; General Review  
LA English  
AB A review. Chronic hepatitis C is caused by infection with the hepatitis C virus (HCV), a member of the Flaviviridae family of viruses. Currently available treatment for HCV, including the standard combination therapy with interferon and ribavirin, is often unsuccessful at eradicating infection. In addition, the therapies now used to treat chronic hepatitis C are associated with substantial side effects. Therefore, new therapeutic strategies such as the use of antiviral drugs targeted to HCV-specific viral enzymes are being explored. One such option is the RNA-directed RNA polymerase (NS5B) inhibitor valopicitabine (NM-283), an orally bioavailable prodrug of the novel ribonucleoside analog NM-107. This compound has shown in vitro activity against HCV-related bovine viral diarrhea virus (BVDV) polymerase. In patients with HCV-1 infection, valopicitabine produced redns. in HCV RNA viral load when administered either as monotherapy or in combination with pegylated interferon. When used together, valopicitabine and interferon appear to have synergistic antiviral effects both in vitro and in vivo. The compound is generally well tolerated, with gastrointestinal effects being the most commonly observed treatment-related adverse events.  
IT 640725-71-9P, NM-283  
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(valopicitabine reduced HCV RNA viral load either as

McIntosh

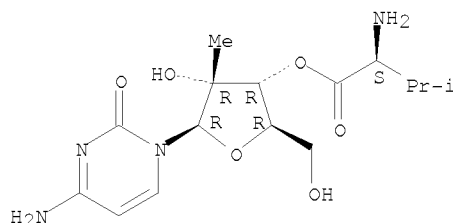
10/609,298

monotherapy or in combination with pegylated interferon against  
HCV-related bovine viral diarrhea virus polymerase and in  
patient with hepatitis C virus-1 infection)

RN 640725-71-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA  
INDEX NAME)

Absolute stereochemistry. Rotation (+).



● 2 HCl

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 24 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2006:425398 CAPLUS

DN 145:39734

TI Nucleoside analog inhibitors of hepatitis C virus  
replication

AU Carroll, S. S.; Olsen, D. B.

CS Department of Antiviral Research, Merck Research Laboratories, West Point,  
PA, 19486, USA

SO Infectious Disorders: Drug Targets (2006), 6(1), 17-29  
CODEN: IDDTAD; ISSN: 1871-5265

PB Bentham Science Publishers Ltd.

DT Journal; General Review

LA English

AB A review. Of the 30 compds. currently marketed in the United States for  
treatment of viral infections, 15 are nucleoside analogs, demonstrating  
the utility of this class of compound as a source of antiviral drugs. The  
success of nucleoside analogs in treating other viral infections provides  
a compelling rationale for the significant effort that is currently being  
devoted to the discovery and development of nucleoside analogs to treat  
infection by hepatitis C virus (HCV) that  
may lead to improvements in response rates compared to currently available  
therapies. Several different approaches were adopted to identify  
promising analogs, including the use of surrogate viruses in cell culture  
assays, screening in the cell-based bicistronic HCV replicon  
assay, and screening nucleoside triphosphates for the ability to inhibit  
the activity of the HCV RNA-dependent RNA polymerase in vitro.  
Several classes of ribonucleoside analogs with modifications of the ribose  
inhibit HCV replication. Nucleoside analogs incorporating a  
2'-C-Me modification are potent inhibitors in the replicon assay in the  
absence of cytotoxicity, and appear to exert their inhibition by acting as  
functional chain terminators of RNA synthesis. NM283, a prodrug of  
2'-C-methylcytidine, has entered clin. trials and demonstrated viral load  
redns. in subjects infected with genotype 1 HCV, a genotype  
known to be difficult to treat effectively with currently approved  
therapies. Overall, results to date offer encouragement that improved  
therapies to treat HCV infection including newly developed  
nucleoside analogs may become available within the next few years.

IT 640725-71-9, NM 283

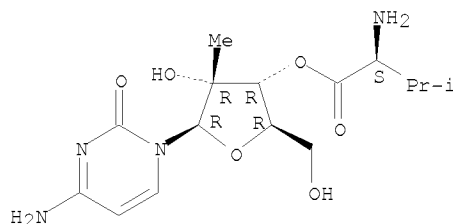
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(nucleoside analog inhibitors of hepatitis C virus  
replication)

RN 640725-71-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA  
INDEX NAME)

McIntosh

Absolute stereochemistry. Rotation (+).



● 2 HCl

RE.CNT 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 25 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2006:342840 CAPLUS

DN 144:381956

TI Combination antiviral compositions comprising castanospermine and use for  
the treatment and prevention of infections caused by or associated with a  
virus of the Flaviviridae family

IN Dugourd, Dominique

PA Migenix Inc., Can.

SO PCT Int. Appl., 54 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006037227	A1	20060413	WO 2005-CA1528	20051006
W:			AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW	
RW:			AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM	
AU 2005291804	A1	20060413	AU 2005-291804	20051006
CA 2583351	A1	20060413	CA 2005-2583351	20051006
US 20060093577	A1	20060504	US 2005-244811	20051006
EP 1802327	A1	20070704	EP 2005-794475	20051006
R:			AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR	
CN 101035555	A	20070912	CN 2005-80034258	20051006
JP 2008515816	T	20080515	JP 2007-534981	20051006
MX 200703853	A	20071121	MX 2007-3853	20070329
KR 2007061879	A	20070614	KR 2007-708715	20070417
IN 2007KN01353	A	20070720	IN 2007-KN1353	20070417
PRAI US 2004-616787P	P	20041006		
WO 2005-CA1528	W	20051006		
AB			The invention discloses the use of castanospermine in combination with another therapeutic agent to treat or prevent infections caused by or associated with a virus of the Flaviviridae family, particularly infections caused by or associated with Hepatitis C virus (HCV), and to the use of such compds. to examine the biol. mechanisms of HCV infection.	
IT 882489-96-5				
RL:			BSU (Biological study, unclassified); BIOL (Biological study) (castanospermine-containing combination antiviral compns., and use for treatment of Flaviviridae infections)	



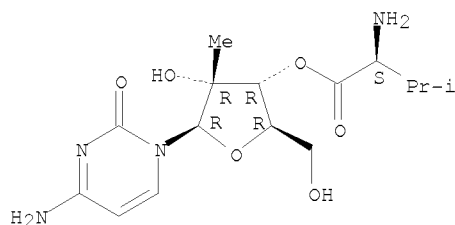
10/609,298

RN 882489-96-5 CAPLUS  
CN L-Valine, 3'-ester with 2'-C-methylcytidine, mixt. with  
(1S,6S,7R,8R,8aR)-octahydro-1,6,7,8-indolizinetetrol (9CI) (CA INDEX  
NAME)

CM 1

CRN 640281-90-9  
CMF C15 H24 N4 O6

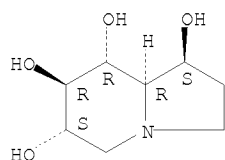
Absolute stereochemistry. Rotation (+).



CM 2

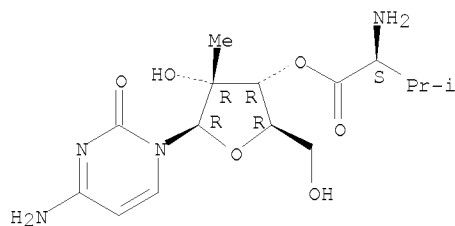
CRN 79831-76-8  
CMF C8 H15 N O4

Absolute stereochemistry. Rotation (+).



IT 640281-90-9, Valopicitabine  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(castanospermine-containing combination antiviral compns., and use for  
treatment of Flaviviridae infections)  
RN 640281-90-9 CAPLUS  
CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 26 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN  
AN 2006:149315 CAPLUS  
DN 144:205728  
TI Methods using a Type II interferon receptor agonist alone or in  
combination with a direct antiviral drug for treating hepatitis  
C virus infection  
IN Blatt, Lawrence M.

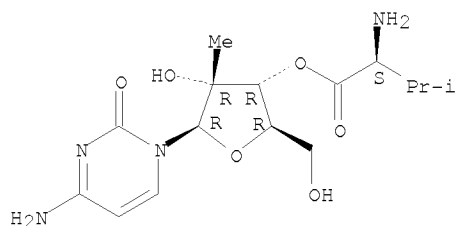
McIntosh

10/609,298

PA Intermune, Inc., USA  
SO PCT Int. Appl., 139 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006016930	A2	20060216	WO 2005-US16927	20050513
	WO 2006016930	A3	20060803		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
	RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
PRAI	US 2004-571322P	P	20040514		
AB	The invention provides methods for treating hepatitis C virus (HCV) infection; methods for reducing the incidence of complications associated with HCV and cirrhosis of the liver; and methods for reducing viral load, or reducing the time to viral clearance, or reducing morbidity or mortality in the clin. outcomes, in patients suffering from HCV infection. The methods generally involve administering to the individual a Type II interferon receptor agonist alone or in combination with a direct antiviral drug.				
IT	640725-71-9, NM 283 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (type II interferon receptor agonist alone or in combination with direct antiviral drug for treating hepatitis C virus infection)				
RN	640725-71-9 CAPLUS				
CN	L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA INDEX NAME)				

Absolute stereochemistry. Rotation (+).



● 2 HCl

L11 ANSWER 27 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN  
AN 2006:103884 CAPLUS  
DN 144:171198  
TI Preparation of alkyl-substituted 2-deoxy-2-fluoro-D-ribofuranosyl pyrimidine and purine nucleoside analogs via condensation of the lactone to nucleosides as potential antiviral agents  
IN Wang, Peiyuan; Stec, Wojciech; Clark, Jeremy; Chun, Byoung-Kwon; Shi, Junxing; Du, Jinfa  
PA Pharmasset, Inc., USA  
SO PCT Int. Appl., 34 pp.  
CODEN: PIXXD2  
DT Patent  
LA English

McIntosh

## FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006012440	A2	20060202	WO 2005-US25916	20050721
	WO 2006012440	A3	20060727		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
	RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	AU 2005267051	A1	20060202	AU 2005-267051	20050721
	CA 2574651	A1	20060202	CA 2005-2574651	20050721
	EP 1773856	A2	20070418	EP 2005-775359	20050721
	R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR			
	CN 101023094	A	20070822	CN 2005-80031530	20050721
	BR 2005012104	A	20080311	BR 2005-12104	20050721
	JP 2008507547	T	20080313	JP 2007-522763	20050721
	US 20060199783	A1	20060907	US 2006-353597	20060213
	MX 200700803	A	20070402	MX 2007-803	20070119
	IN 2007KN00605	A	20070706	IN 2007-KN605	20070220
	KR 2007114344	A	20071203	KR 2007-703980	20070220
PRAI	US 2004-589866P	P	20040721		
	US 2004-608320P	P	20040909		
	US 2005-185988	A1	20050721		
	WO 2005-US25916	W	20050721		
OS	MARPAT 144:171198				
GI					

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB A process for preparing of 2-deoxy-2-fluoro-2-methyl-D-ribonolactones, I, wherein R1 and R2 can independently be H, CH3, acetyl, benzoyl, pivaloyl, 4-nitrobenzoyl, 3-nitrobenzoyl, 2-nitrobenzoyl, 4-chlorobenzoyl, 3-chlorobenzoyl, 2-chlorobenzoyl, 4-methylbenzoyl, 3-methylbenzoyl, 2-methylbenzoyl, 4-phenylbenzoyl, benzyl, 4-methoxybenzyl, trityl, trialkylsilyl, t-butyl-dialkylsilyl, t-butyldiphenylsilyl, TIPDS, THP, MOM, or MEM are prepared and used in the condensation to 2-deoxy-2-fluoro-D-ribofuranosyl pyrimidine and purine nucleoside analogs. Thus, 2-deoxy-2-fluoro-D-ribofuranosyl pyrimidine and purine nucleoside analogs II and III, wherein X is a halogen; Y is N or CH; Z is a halogen, hydroxyl, ether, thiol, thioether, (un)substituted amine or alkyl; R1' is alkyl, vinyl, ethynyl; R2' and R3' can be same or different H, alkyl, arylalkyl, acyl, cyclic acetal such as 2',3'-O-isopropylidene or 2',3'-O-benzylidene, or 2',3'-cyclic carbonate; R4, R5, and R6 are independently H, halogen, hydroxyl, ether, thiol, thioether, N3, (un)substituted amine, (un)substituted amido, alkyl, halogenated alkyl, alkenyl, halogenated alkenyl, alkynyl, halogenated alkynyl, hydroxy alkyl, alkoxy are prepared and are potential anti-HCV agents. Specifically, IV was prepared (no yield, claimed) via condensation, alkylation and stereoselective fluorination reactions and can exhibit potential use as an anti-HCV agent.

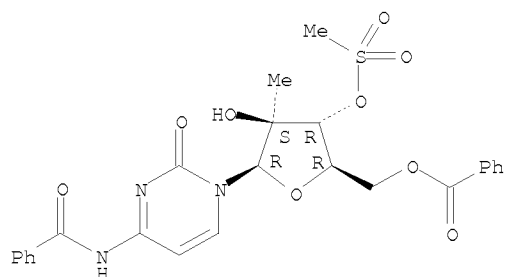
IT 874638-81-0P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of alkyl-substituted 2-deoxy-2-fluoro-D-ribofuranosyl pyrimidine and purine nucleoside analogs via condensation of the lactone to nucleosides)

RN 874638-81-0 CAPLUS

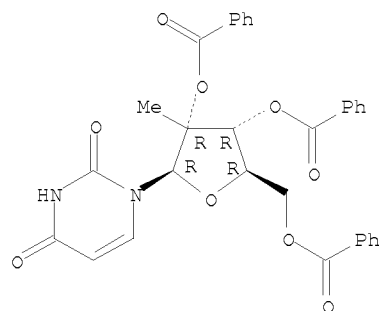
CN Benzamide, N-[1-[5-O-benzoyl-2-C-methyl-3-O-(methylsulfonyl)-β-D-arabinofuranosyl]-1,2-dihydro-2-oxo-4-pyrimidinyl]- (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 28 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN  
 AN 2005:1151389 CAPLUS  
 DN 145:271979  
 TI NM 283, an efficient prodrug of the potent anti-HCV agent 2'-C-methylcytidine  
 AU Pierra, C.; Benzaria, S.; Amador, A.; Moussa, A.; Mathieu, S.; Storer, R.; Gosselin, G.  
 CS Laboratoire Cooperatif Idenix, CNRS, Universite Montpellier II, Montpellier, 5, Fr.  
 SO Nucleosides, Nucleotides & Nucleic Acids (2005), 24(5-7), 767-770  
 CODEN: NNAFY; ISSN: 1525-7770  
 PB Taylor & Francis, Inc.  
 DT Journal  
 LA English  
 OS CASREACT 145:271979  
 AB In order to improve the oral bioavailability of 2'-C-methylcytidine, a potent anti-HCV agent, the corresponding 3'-O-L-valinyl ester derivative (NM 283) has been synthesized. Based on its ease of synthesis and its physicochem. properties, NM 283 has emerged as a promising antiviral drug for treatment of chronic HCV infection.  
 IT 23643-36-9P 640725-70-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of NM 283 as efficient prodrug of potent anti-HCV agent 2'-C-methylcytidine)  
 RN 23643-36-9 CAPLUS  
 CN 2,4(1H,3H)-Pyrimidinedione, 1-(2,3,5-tri-O-benzoyl-2-C-methyl-β-D-ribofuranosyl)- (9CI) (CA INDEX NAME)

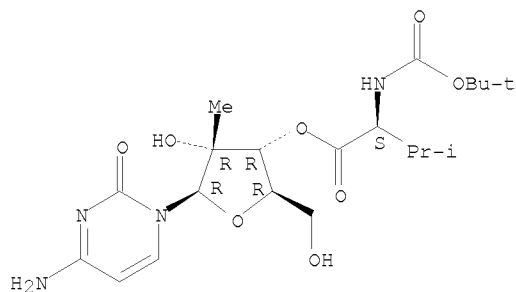
Absolute stereochemistry.



RN 640725-70-8 CAPLUS  
 CN L-Valine, N-[(1,1-dimethylethoxy)carbonyl]-, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry.

10/609,298



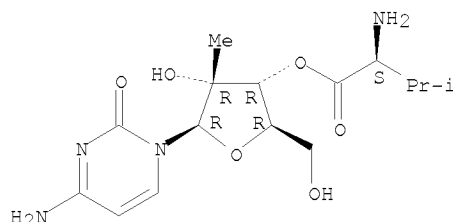
IT 640725-71-9P

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use);  
BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prodrug; preparation of NM 283 as efficient prodrug of potent anti-  
HCV agent 2'-C-methylcytidine)

RN 640725-71-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA  
INDEX NAME)

Absolute stereochemistry. Rotation (+).



● 2 HCl

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 29 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2005:684531 CAPLUS

DN 143:431740

TI Emerging drugs for chronic hepatitis C

AU Bhopale, Girish Mahadeorao; Nanda, Rabindra Kumar

CS Research and Development Division, Hindustan Antibiotics Limited, Pimpri,  
Pune, 411018, India

SO Hepatology Research (2005), 32(3), 146-153

CODEN: HPRSEFM; ISSN: 1386-6346

PB Elsevier B.V.

DT Journal; General Review

LA English

AB A review. Hepatitis C virus (HCV) is a major cause of chronic hepatitis, liver cirrhosis and hepatocellular carcinoma worldwide. A combination therapy comprising pegylated interferon and ribavirin currently represents the most effective therapy for chronic HCV infection. The limitations of this current therapy mainly its efficacy and significant side effects have prompted the development of new drugs. Few categories of therapeutic agents appear promising for future therapy, e.g. novel interferons, ribavirin analogs, antisense oligonucleotides, short interfering RNAs, ribozymes, enzyme inhibitors, immunomodulatory agents, antifibrotic agents, therapeutic vaccines and antibodies. Few drugs belong to afore-mentioned categories have already reached the different clin. phases of development. The present article highlights the status of current available therapies and emerging drugs for the treatment of hepatitis C.

IT 640725-71-9, NM 283

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

McIntosh

10/609,298

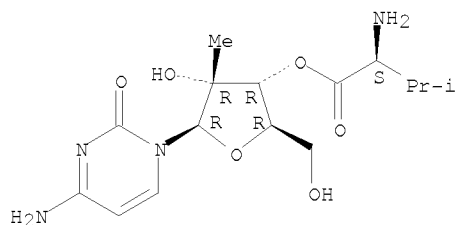
(Biological study); USES (Uses)

(NM283 proved promising therapeutic effect in treating chronic hepatitis C patient)

RN 640725-71-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



● 2 HCl

RE.CNT 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 30 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2005:648160 CAPLUS

DN 143:248607

TI Design, Synthesis, and Antiviral Activity of 2'-Deoxy-2'-fluoro-2'-C-methyl-cytidine, a Potent Inhibitor of Hepatitis C Virus Replication

AU Clark, Jeremy L.; Hollecker, Laurent; Mason, J. Christian; Stuyver, Lieven J.; Tharnish, Phillip M.; Lostia, Stefania; McBrayer, Tamara R.; Schinazi, Raymond F.; Watanabe, Kyoichi A.; Otto, Michael J.; Furman, Phillip A.; Stec, Wojciech J.; Patterson, Steven E.; Pankiewicz, Krzysztof W.

CS Pharmasset, Inc., Princeton, NJ, 08540, USA

SO Journal of Medicinal Chemistry (2005), 48(17), 5504-5508

CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

OS CASREACT 143:248607

AB The pyrimidine nucleoside-  $\beta$ -D-2'-deoxy-2'-fluoro-2'-C-methylcytidine (I) was designed as a hepatitis C virus RNA-dependent RNA polymerase (HCV RdRp) inhibitor. The title compound was obtained by a DAST fluorination of N4-benzoyl-1-(2-methyl-3,5-di-O-benzoyl- $\beta$ -D-arabinofuranosyl)cytosine to provide N4-benzoyl-1-(2-fluoro-2-methyl-3,5-di-O-benzoyl- $\beta$ -D-ribofuranosyl)cytosine. The protected 2'-C-methylcytidine was obtained as a byproduct from the DAST fluorination and allowed for the preparation of two biol. active compds. from a common precursor. Compound I and 2'-C-methylcytidine were assayed in a sub-genomic HCV replicon assay system and found to be potent and selective inhibitors of HCV replication. Compd.I shows increased inhibitory activity in the HCV replicon assay compared to 2'-C-methylcytidine and low cellular toxicity.

IT 863329-62-8P 863329-64-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(design, synthesis via fluorination, and antiviral activity of 2'-deoxy-2'-fluoro-2'-C-methyl-cytidine, a potent inhibitor of Hepatitis C virus replication)

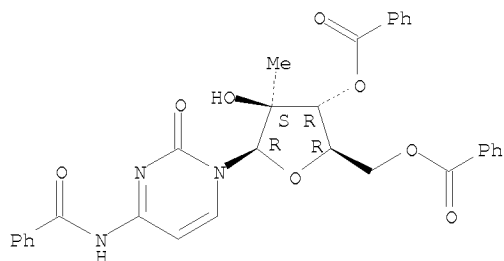
RN 863329-62-8 CAPLUS

CN Benzamide, N-[1-(3,5-di-O-benzoyl-2-C-methyl- $\beta$ -D-arabinofuranosyl)-1,2-dihydro-2-oxo-4-pyrimidinyl]- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

McIntosh

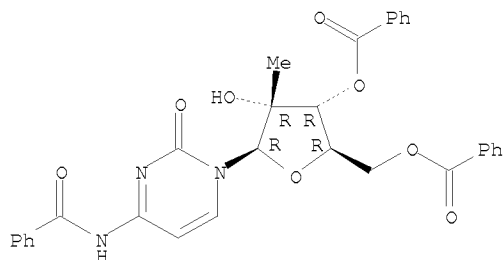
10/609,298



RN 863329-64-0 CAPLUS

CN Cytidine, N-benzoyl-2'-C-methyl-, 3',5'-dibenzoate (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 31 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2005:34765 CAPLUS

DN 142:94074

TI Preparation of modified fluorinated (2'R)-2'-deoxy-2'-fluoro-2'-C-methyl nucleoside analogs as antiviral agents

IN Clark, Jeremy

PA Pharmasset, Ltd., Barbados

SO PCI Int. Appl., 228 pp.

CODEN: PIXXD2

DT Patent

LA English

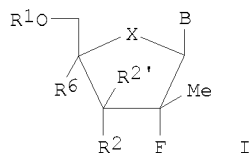
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005003147	A2	20050113	WO 2004-US12472	20040421
	WO 2005003147	A3	20050303		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
	RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	AU 2004253860	A2	20050113	AU 2004-253860	20040421
	AU 2004253860	A1	20050113		
	CA 2527657	A1	20050113	CA 2004-2527657	20040421
	US 20050009737	A1	20050113	US 2004-828753	20040421
	EP 1633766	A2	20060315	EP 2004-775900	20040421
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR			
	BR 2004010846	A	20060627	BR 2004-10846	20040421
	CN 1816558	A	20060809	CN 2004-80019148	20040421
	JP 2006526629	T	20061124	JP 2006-513231	20040421
	MX 2005PA12788	A	20060222	MX 2005-PA12788	20051125
	IN 2005DN06087	A	20080509	IN 2005-DN6087	20051227

McIntosh

10/609,298

	NO 2005006221	A	20051228	NO 2005-6221	20051228
	US 20080070861	A1	20080320	US 2007-854218	20070912
PRAI	US 2003-474368P	P	20030530		
	US 2004-828753	A3	20040421		
WO	2004-US12472	W	20040421		
OS	MARPAT 142:94074				
GI					



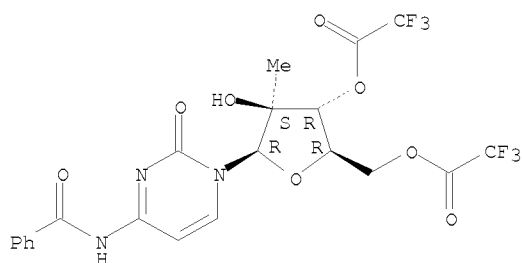
AB The disclosed invention provides nucleoside analogs I, wherein B is purine and pyrimidine nucleobase; X is O, S, CH<sub>2</sub>, Se, NH, N-alkyl, CHW, C(W)<sub>2</sub>; W is F, Cl, Br, iodo; R<sub>1</sub> is H, phosphate, H-phosphonate, acyl, Ph, alkyl, carboxyalkylamino, sulfonate ester, peptide, amino acid, sugar residue; R<sub>2</sub> and R<sub>2</sub>' are independently H, alkyl, alkenyl, alkynyl, vinylyl, N<sub>3</sub>, CN, halogen, NO<sub>2</sub>, ester, alkoxy, thioalkyl, sulfoxide, sulfonyl; R<sub>6</sub> is alkyl, CN, Me, OMe, OEt, CH<sub>2</sub>OH, CH<sub>2</sub>F, N<sub>3</sub>, CHCN, CH<sub>2</sub>N<sub>3</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NHMe, CH<sub>2</sub>NMe<sub>2</sub>, alkylne; and methods of treating a Flaviviridae infection, including hepatitis C virus, West Nile Virus, yellow fever virus, and a rhinovirus infection in a host, including animals, and especially human, using a (2'R)-2'-deoxy-2'-fluoro-2'-C-Me nucleosides, or a pharmaceutically acceptable salt or prodrug thereof. Thus, (2'R)-2'-deoxy-2'-fluoro-2'-C-methylcytidine was prepared and tested as antiviral agent. The effects the nucleoside analogs tested on human bone marrow cells are reported. (2'R)-2'-deoxy-2'-fluoro-2'-C-methylcytidine shows activity against Rhinovirus, West Nile virus, Yellow Fever virus, and Dengue virus. Cytotoxicity and effect of nucleoside analogs on human bone marrow cells are reported.

IT 817204-36-7P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of modified fluorinated (2'R)-2'-deoxy-2'-fluoro-2'-C-Me nucleoside analogs as antiviral agents)

RN 817204-36-7 CAPLUS

CN Benzamide, N-[1,2-dihydro-1-[2-C-methyl-3,5-bis-O-(trifluoroacetyl)-β-D-arabinofuranosyl]-2-oxo-4-pyrimidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 32 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2004:780543 CAPLUS

DN 141:296247

TI Preparation of cytidine nucleoside analogs as antiviral agents

IN Girardet, Jean-Luc; Koh, Yung-Hyo; An, Haoyun; Hong, Zhi

PA Ribapharm Inc., USA

SO PCT Int. Appl., 59 pp.  
CODEN: PIXXD2

DT Patent

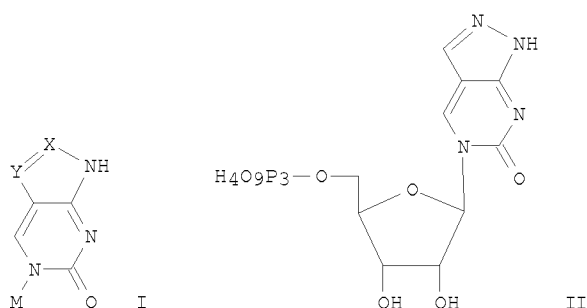
LA English

FAN.CNT 1

McIntosh



	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	WO 2004080466	A1	20040923	WO 2003-US6992	20030307
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	AU 2003225705	A1	20040930	AU 2003-225705	20030307
PRAI	WO 2003-US6992	A	20030307		
OS	MARPAT 141:296247				
GI					



AB Cytidine analogs I, wherein -X=Y- is -N=N-, -CH=N-, -N=CZ- or -CH=CZ-, wherein Z is H, halogen, or alkyl, and wherein M is a sugar or sugar analog; wherein the compound has a D-configuration or an L-configuration; with the proviso that where M is a substituted sugar with a ribofuranose ring having a heteroatom and substituents R1 and R2 on the C3'-atom, R3 and R4 on the C2'-atom, and R5 on the C5'-atom, R1-R4 together are not independently H, OH, F, NH2, N3, O-hydrocarbyl, or a reporter moiety, when the heteroatom is O, S, Se, SO, N-alkyl, or CH2, and when R5 is OH, SH, NH2, monophosphate, diphosphate, triphosphate, thiophosphate, or boranophosphate; and with the further proviso that M does not comprise a cyclopentenyl group, a morpholino group, or M is not a phosphonylmethoxyethyl, their prodrugs and/or metabolites are employed as pharmaceutically active compds. for treatment of diseases responsive to such compds. Particularly preferred diseases include viral diseases (e.g., HCV infection) and neoplasms (no biol. data). Thus nucleoside analog II was prepared and tested as antiviral agent. The virus is an HCV virus, an HIV virus, an RSV virus, an influenza virus, or a an HBV virus.

IT 23643-36-9

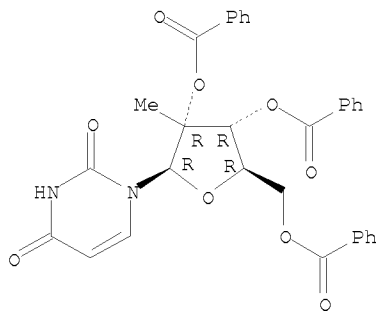
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of cytidine nucleoside analogs as antiviral agents)

RN 23643-36-9 CAPLUS

2,4(1H,3H)-Pyrimidinedione, 1-(2,3,5-tri-O-benzoyl-2-C-methyl- $\beta$ -D-ribofuranosyl)- (9CI) (CA INDEX NAME)

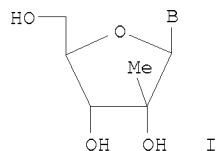
Absolute stereochemistry.



RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 33 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN  
AN 2004:566635 CAPLUS  
DN 141:89323  
TI Process for the production of 3'-nucleoside prodrugs  
IN Storer, Richard; Moussa, Adel; Mathieu, Steven; Qu, Lin  
PA Idenix Cayman Limited, Cayman I.  
SO PCT Int. Appl., 57 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004058792	A1	20040715	WO 2003-US41603	20031223
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RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2511616	A1	20040715	CA 2003-2511616	20031223
AU 2003300434	A1	20040722	AU 2003-300434	20031223
US 20040181051	A1	20040916	US 2003-746395	20031223
EP 1575971	A1	20050921	EP 2003-814400	20031223
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BR 2003016868	A	20051025	BR 2003-16868	20031223
CN 1751058	A	20060322	CN 2003-80109820	20031223
JP 2006514038	T	20060427	JP 2004-562599	20031223
NZ 540913	A	20080229	NZ 2003-540913	20031223
ZA 2005005040	A	20060426	ZA 2005-5040	20050621
NO 2005003557	A	20050908	NO 2005-3557	20050720
PRAI US 2002-436150P	P	20021223		
WO 2003-US41603	W	20031223		
OS CASREACT 141:89323; MARPAT 141:89323				
GI				

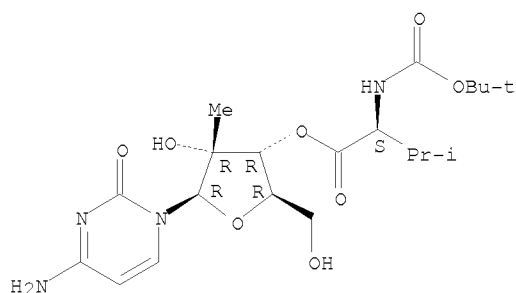


AB Provided is a single-step process for the regioselective 3'-acylation of a ribofuranosyl 2'- or 3'-branched nucleosides I, wherein B is nucleobase.

These compds. are useful as antiviral agents, and in particular, can be used to treat Flaviviridae infections in a host in need thereof (no data). Thus, 9-(2'-C-methyl-3'-O-valinoyl- $\beta$ -D-ribofuranosyl)-6-N-methyladenine dihydrochloride was prepared via regioselective esterification of 9-(2'-C-methyl- $\beta$ -D-ribofuranosyl)-6-N-methyladenine with N-(tert-butoxycarbonyl)-L-valine.

IT 640725-70-8P  
 RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)  
 (process for production of nucleoside prodrugs via regioselective esterification)  
 RN 640725-70-8 CAPLUS  
 CN L-Valine, N-[(1,1-dimethylethoxy)carbonyl]-, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 34 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN  
 AN 2004:453348 CAPLUS  
 DN 141:17578  
 TI Treatment of Flaviviridae infection with 2'-branched nucleosides and another mutation-inducing drug such as interferon  
 IN Sommadossi, Jean-Pierre; La Colla, Paolo; Standring, David; Bichko, Vadim; Qu, Lin  
 PA Idenix (Cayman) Limited, Cayman I.; Universita Degli Studi Di Cagliari  
 SO PCI Int. Appl., 166 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004046331	A2	20040603	WO 2003-US36714	20031117
WO 2004046331	A3	20060302		
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RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2506129	A1	20040603	CA 2003-2506129	20031117
AU 2003298658	A1	20040615	AU 2003-298658	20031117
US 20050031588	A1	20050210	US 2003-715729	20031117
EP 1576138	A2	20050921	EP 2003-796412	20031117
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
BR 2003016363	A	20051004	BR 2003-16363	20031117
JP 2006519753	T	20060831	JP 2004-553823	20031117
CN 1849142	A	20061018	CN 2003-80108747	20031117
MX 2005PA05192	A	20050908	MX 2005-PA5192	20050513
NO 2005002920	A	20050815	NO 2005-2920	20050615
PRAI US 2002-426675P	P	20021115		
WO 2003-US36714	W	20031117		

OS MARPAT 141:17578

AB The present invention discloses a method for the treatment of Flaviviridae infection that includes the administration of a 2'-branched nucleoside, or a pharmaceutically acceptable prodrug and/or salt thereof, to a human in need of therapy in combination or alternation with a drug that directly or indirectly induces a mutation in the viral genome at a location other than a mutation of a nucleotide that results in a change from serine to a different amino acid in the highly conserved consensus sequence,  $\text{XRX}\langle\text{u}\rangle\text{S}\langle\text{u}\rangle\text{GXXX}\text{T}$ , of domain B of the RNA polymerase region, or is associated with such a mutation. The invention also includes a method to detect a mutant strain of Flaviviridae and a method for its treatment. Thus, in bovine viral diarrhea virus (BVDV)-infected MDBK cells treated with  $\beta$ -D-2'-methylcytidine, viruses resistant to the nucleoside appeared. The drug resistance was associated with a mutation in the NS5B gene which resulted in an S405T substitution in the encoded RNA-dependent RNA polymerase. These mutant viruses were sensitive to Intron A (interferon  $\alpha$ -2b). Intron A and  $\beta$ -D-2'-methylcytidine exhibited synergistic inhibitory activity on BVDV growth in MDBK cells.

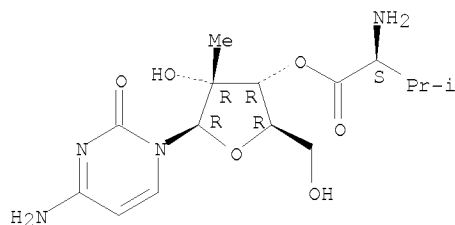
IT 640281-90-9

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(treatment of Flaviviridae infection with 2'-branched nucleosides and another mutation-inducing drug such as interferon)

RN 640281-90-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L11 ANSWER 35 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2004:20697 CAPLUS

DN 140:87662

TI 2'- and 3'-nucleoside prodrugs for treating Flaviviridae infections

IN Sommadossi, Jean-pierre; La Colla, Paolo; Storer, Richard; Gosselin, Gilles

PA Idenix (Cayman) Limited, Cayman I.; Centre National de la Recherche Scientifique; Universita Degli Studi di Cagliari

SO PCT Int. Appl., 2498 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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	WO 2004003000	A3	20041104		
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	AU 2003263412	A1	20040119	AU 2003-263412	20030627
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CN 1678621	A	20051005	CN 2003-820690	20030627
JP 2005537242	T	20051208	JP 2004-517162	20030627
CN 1761677	A	20060419	CN 2003-820501	20030627
US 20070087960	A1	20070419	US 2003-608907	20030627
BR 2003012271	A	20071106	BR 2003-12271	20030627
CN 101172992	A	20080507	CN 2007-10193301	20030627
CN 101172993	A	20080507	CN 2007-10199501	20030627
WO 2005020884	A2	20050310	WO 2004-US15395	20040514
WO 2005020884	A3	20060622		
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US 20070032449	A1	20070208	US 2004-5441	20041206
US 20070032407	A1	20070208	US 2004-5473	20041206
US 7192936	B2	20070320		
US 20070037735	A1	20070215	US 2004-5442	20041206
US 20070042939	A1	20070222	US 2004-5445	20041206
US 20070042991	A1	20070222	US 2004-5447	20041206
US 7365057	B2	20080429		
US 20070042940	A1	20070222	US 2004-5467	20041206
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MX 2004PA12779	A	20050819	MX 2004-PA12779	20041216
NO 2005000466	A	20050323	NO 2005-466	20050127
IN 2005DN00341	A	20070202	IN 2005-DN341	20050128
US 20070275883	A1	20071129	US 2006-516928	20060906
PRAI US 2002-392350P	P	20020628		
US 2002-392351P	P	20020628		
US 2003-466194P	P	20030428		
US 2003-470949P	P	20030514		
CN 2003-820501	A3	20030627		
CN 2003-820701	A3	20030627		
US 2003-607909	A1	20030627		
US 2003-608907	A1	20030627		
US 2003-609298	A1	20030627		
WO 2003-IB3901	W	20030627		
WO 2004-US15395	W	20040514		
OS MARPAT 140:87662				
AB	2' And 3'-Prodrugs of 1'-, 2'-, 3'-, or 4'-branched $\beta$ -D or $\beta$ -L nucleosides, or their pharmaceutically acceptable salts and derivs., are described which are useful in the prevention and treatment of Flaviviridae infections and other related conditions. These modified nucleosides provide superior results against flaviviruses and pestiviruses, including hepatitis C virus and viruses generally that replicate through an RNA-dependent RNA reverse transcriptase. Compds., compns., methods and uses are provided for the treatment of Flaviviridae infection, including HCV infection, that include the administration of an effective amount of the prodrugs of the invention, or their pharmaceutically acceptable salts or derivs. These drugs may optionally be administered in combination or alternation with further antiviral agents to prevent or treat Flaviviridae infections and other related conditions. Preparation of compds. of the invention is included.			
IT 640725-71-9P				
	RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic			

10/609,298

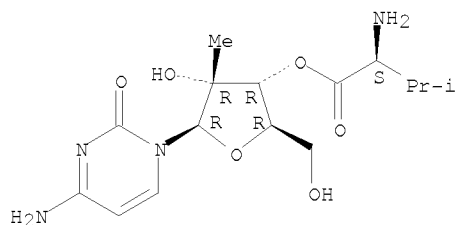
preparation); THU (Therapeutic use); BIOL (Biological study); PREP  
(Preparation); USES (Uses)

(nucleoside prodrugs for treating Flaviviridae infections)

RN 640725-71-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA  
INDEX NAME)

Absolute stereochemistry. Rotation (+).



● 2 HCl

IT 640725-69-5P 640725-70-8P

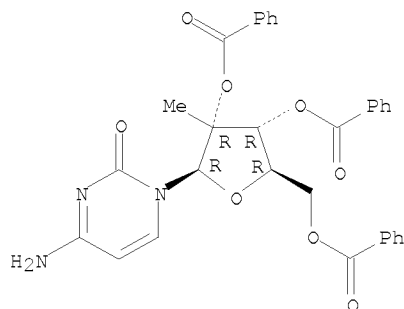
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)

(nucleoside prodrugs for treating Flaviviridae infections)

RN 640725-69-5 CAPLUS

CN Cytidine, 2'-C-methyl-, 2',3',5'-tribenzoate (9CI) (CA INDEX NAME)

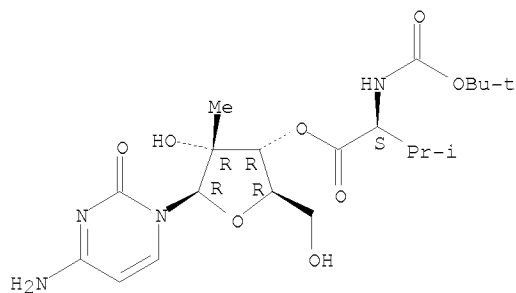
Absolute stereochemistry.



RN 640725-70-8 CAPLUS

CN L-Valine, N-[(1,1-dimethylethoxy)carbonyl]-, 3'-ester with  
2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 36 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN

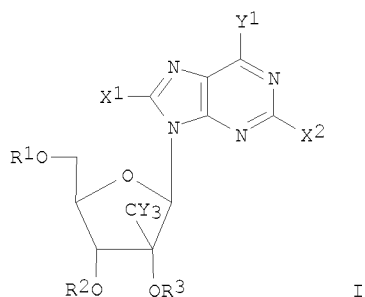
McIntosh

AN 2004:20696 CAPLUS  
 DN 140:77365  
 TI Preparation of modified 2'- and 3'-nucleoside prodrugs for treating  
 Flaviviridae infections  
 IN Sommadossi, Jean-pierre; La Colla, Poalo; Storer, Richard; Gosselin,  
 Gilles  
 PA Idenix (Cayman) Limited, Cayman I.; Universita degli studi di Cagliari;  
 Centre National de la Recherche Scientifique  
 SO PCT Int. Appl., 201 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 4

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	CA 2490191	A1	20040108	CA 2003-2490191	20030627
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	CN 1678621	A	20051005	CN 2003-820690	20030627
	JP 2005533817	T	20051110	JP 2004-517158	20030627
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	US 20070087960	A1	20070419	US 2003-608907	20030627
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	CN 101172992	A	20080507	CN 2007-10193301	20030627
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	US 20070032449	A1	20070208	US 2004-5441	20041206
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	US 20070037735	A1	20070215	US 2004-5442	20041206
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	US 20070042990	A1	20070222	US 2004-5471	20041206
	US 20070060503	A1	20070315	US 2004-5440	20041206
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	US 20070060504	A1	20070315	US 2004-5446	20041206
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	US 20070060505	A1	20070315	US 2004-5472	20041206
	MX 2004PA12709	A	20050930	MX 2004-PA12709	20041215

10/609,298

	NO 2005000465	A	20050127	NO 2005-465	20050127
	US 20070275883	A1	20071129	US 2006-516928	20060906
PRAI	US 2002-392350P	P	20020628		
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	US 2003-466194P	P	20030428		
	US 2003-470949P	P	20030514		
	CN 2003-820501	A3	20030627		
	CN 2003-820701	A3	20030627		
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OS	MARPAT 140:77365				
GI					



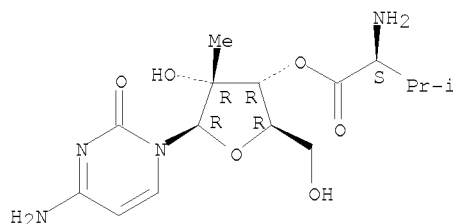
AB 2' And/or 3' prodrugs of 1', 2', 3' or 4'-branched-nucleosides I, wherein R1-R3 are independently H, phosphate, alkyl, acyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, CO-aryloxyalkyl, CO-substituted aryl, sulfonate ester, benzyl, wherein the Ph group is optionally substituted with one or more substituents, alkylsulfonyl, arylsulfonyl, aralkylsulfonyl, lipid, amino acid, carbohydrate, peptide, cholesterol; Y1 is hydrogen, bromo, chloro, fluoro, iodo, CN, OH, OR4, NH2, NHR4, NR4R5, SH or SR4; X1 and X2 are independently alkyl, CH3, CF3, CY3, 2-Br-Et, CH2F, CH2Cl, CH2CF3, CF2CF3, CY2CY3, CH2OH, alkenyl, alkynyl, COOH, COOR4, COO-alkyl, COO-aryl, CO-O-alkoxyalkyl, CONH2, CONHR4, CON(R4)2, halo, CN, N3, OH, OR4, NH2, NHR4, NR4R5, SH or SR5; Y is independently H, halo; and each R4 and R5 is independently hydrogen, acyl, alkyl, lower alkyl, alkenyl, alkynyl or cycloalkyl, and their pharmaceutically acceptable salts and derivs. are described. These prodrugs are useful in the prevention and treatment of Flaviviridae infections, including HCV infection, and other related conditions. Compds. and compns. of the prodrugs of the present invention are described. Methods and uses are also provided that include the administration of an effective amount of the prodrugs of the present invention, or their pharmaceutically acceptable salts or derivs. These drugs may optionally be administered in combination or alteration with further anti-viral agents to prevent or treat Flaviviridae infections and other related conditions. Thus, antiviral activity of  $\beta$ -D-2'-C-methyl-7-methyl-6-phenyl-3,3a,5,8a-tetrahydro-1,3,4,5,7a-penta-aza-s-indacen-8-one is reported.

IT 640281-90-9P  
 RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of modified and nucleoside prodrugs for treating flaviviridae infections)

RN 640281-90-9 CAPLUS  
 CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



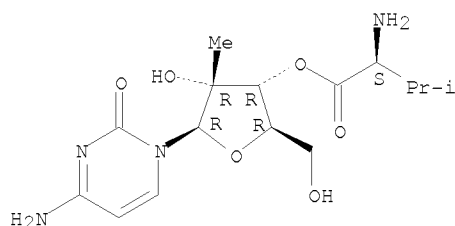


L11 ANSWER 37 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN  
 AN 2004:20443 CAPLUS  
 DN 140:70984  
 TI 2'-C-methyl-3'-O-L-valine ester ribofuranosyl cytidine for treatment of  
 flaviviridae infections  
 IN Sommadossi, Jean-Pierre; La Colla, Paolo  
 PA Idenix (Cayman) Limited, Cayman I.; Universita Degli Studi di Cagliari  
 SO PCT Int. Appl., 110 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004002422	A2	20040108	WO 2003-US20431	20030627
WO 2004002422	A3	20050407		
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AU 2003248748	A1	20040119	AU 2003-248748	20030627
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US 20070032449	A1	20070208	US 2004-5441	20041206
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	US 20070042991	A1	20070222	US 2004-5447	20041206
	US 7365057	B2	20080429		
	US 20070042940	A1	20070222	US 2004-5467	20041206
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	US 20070060503	A1	20070315	US 2004-5440	20041206
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	WO 2004-US15395	W	20040514		
	IN 2005-DN344	A3	20050128		
OS	MARPAT 140:70984				
AB	The 3'-L-valine ester of $\beta$ -D-2'-C-methyl-ribofuranosyl cytidine provides superior results against flaviviruses and pestiviruses, including hepatitis C virus. Based on this discovery, compds., compns., methods and uses are provided for the treatment of flaviviridae, including HCV, that include the administration of an effective amount of val-mCyd or its salt, ester, prodrug or derivative, optionally in a pharmaceutically acceptable carrier. In an alternative embodiment, val-mCyd is used to treat any virus that replicates through an RNA-dependent RNA polymerase. Several examples are provided of the pharmacol., mechanism of action, metabolism, side effects, and clin. efficacy of the title compound				
IT	640281-90-9D, salts 642075-50-1 642075-51-2 642075-52-3 642075-53-4 642075-54-5 642075-55-6 642075-56-7 642075-57-8 642075-58-9 642075-59-0 642075-60-3 642075-61-4 642075-62-5 642075-63-6 642075-64-7 642075-65-8 642075-66-9 642075-67-0 642075-68-1 642075-69-2 642075-70-5 642075-71-6 642075-72-7 642075-74-9 642075-75-0 642075-76-1 642075-77-2 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (ribofuranosylcytidine methylvaline ester combined with other antivirals for treatment of flaviviridae infections)				
RN	640281-90-9 CAPLUS				
CN	L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)				

Absolute stereochemistry. Rotation (+).



RN 642075-50-1 CAPLUS  
CN L-Valine, 3'-ester with 2'-C-methylcytidine, 4-methylbenzenesulfonate (salt) (9CI) (CA INDEX NAME)

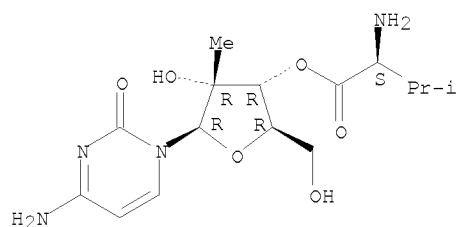
10/609,298

CM 1

CRN 640281-90-9

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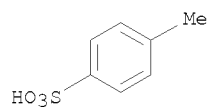
Absolute stereochemistry. Rotation (+).



CM 2

CRN 104-15-4

CMF C7 H8 O3 S



RN 642075-51-2 CAPLUS

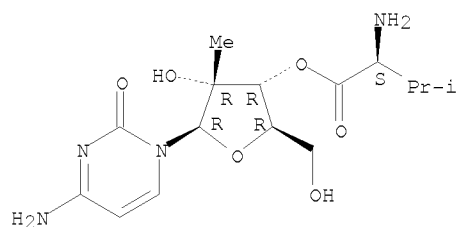
CN L-Valine, 3'-ester with 2'-C-methylcytidine, methanesulfonate (salt) (9CI)  
(CA INDEX NAME)

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

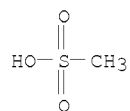
Absolute stereochemistry. Rotation (+).



CM 2

CRN 75-75-2

CMF C H4 O3 S



RN 642075-52-3 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, acetate (salt) (9CI) (CA

McIntosh

10/609,298

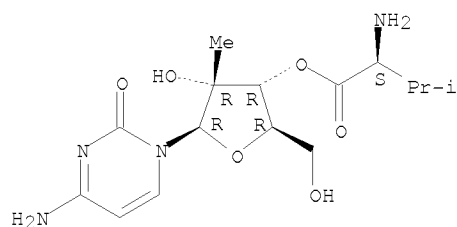
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CRN 640281-90-9

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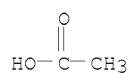
Absolute stereochemistry. Rotation (+).



CM 2

CRN 64-19-7

CMF C2 H4 O2



RN 642075-53-4 CAPLUS

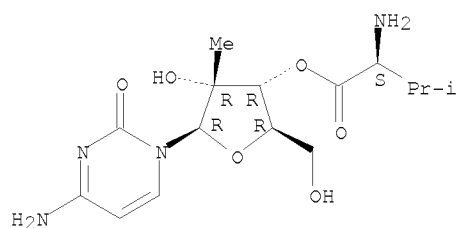
CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2-hydroxy-1,2,3-propanetricarboxylate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

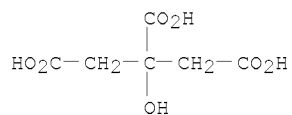
Absolute stereochemistry. Rotation (+).



CM 2

CRN 77-92-9

CMF C6 H8 O7



RN 642075-54-5 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, propanedioate (salt) (9CI) (CA INDEX NAME)

McIntosh

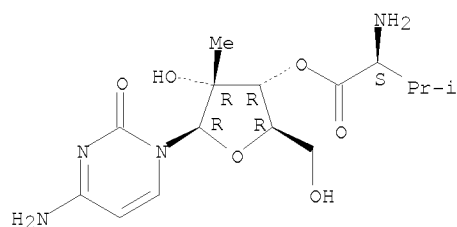
10/609,298

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

CRN 141-82-2

CMF C3 H4 O4

HO<sub>2</sub>C—CH<sub>2</sub>—CO<sub>2</sub>H

RN 642075-55-6 CAPLUS

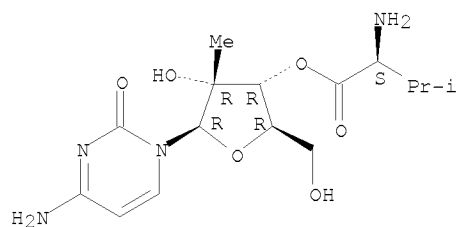
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CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).

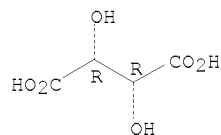


CM 2

CRN 87-69-4

CMF C4 H6 O6

Absolute stereochemistry.



RN 642075-56-7 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, butanedioate (salt) (9CI) (CA INDEX NAME)

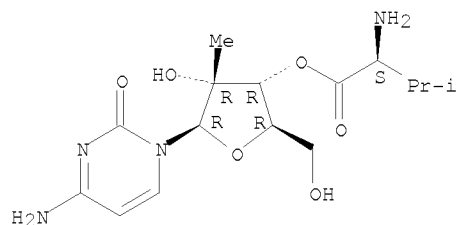
McIntosh

10/609,298

CM 1

CRN 640281-90-9  
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

CRN 110-15-6  
CMF C4 H6 O4

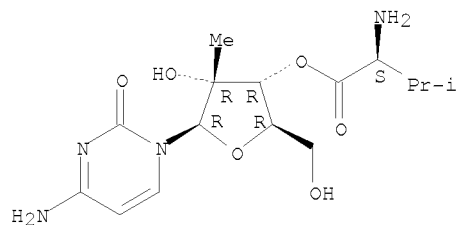
HO<sub>2</sub>C-CH<sub>2</sub>-CH<sub>2</sub>-CO<sub>2</sub>H

RN 642075-57-8 CAPLUS  
CN L-Valine, 3'-ester with 2'-C-methylcytidine, benzoate (salt) (9CI) (CA INDEX NAME)

CM 1

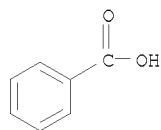
CRN 640281-90-9  
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

CRN 65-85-0  
CMF C7 H6 O2



RN 642075-58-9 CAPLUS  
CN L-Ascorbic acid, compd. with L-valine 3'-ester with 2'-C-methylcytidine (9CI) (CA INDEX NAME)

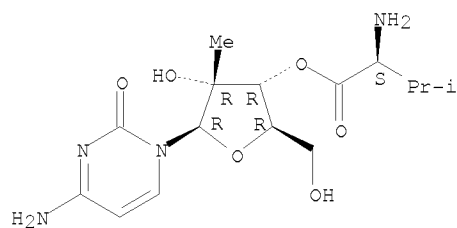
CM 1

McIntosh

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CRN 640281-90-9  
CMF C15 H24 N4 O6

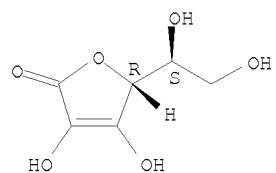
Absolute stereochemistry. Rotation (+).



CM 2

CRN 50-81-7  
CMF C6 H8 O6

Absolute stereochemistry.

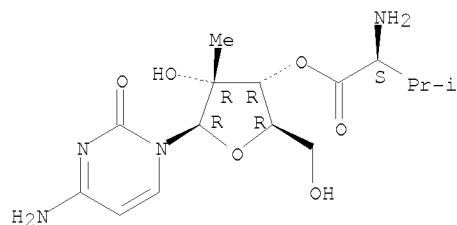


RN 642075-59-0 CAPLUS  
CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2-oxopentanedioate (salt)  
(9CI) (CA INDEX NAME)

CM 1

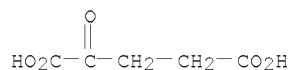
CRN 640281-90-9  
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

CRN 328-50-7  
CMF C5 H6 O5



RN 642075-60-3 CAPLUS  
CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2,3-dihydroxypropyl phosphate  
(salt) (9CI) (CA INDEX NAME)

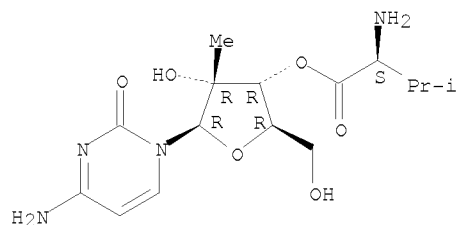
McIntosh

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CM 1

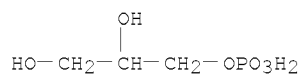
CRN 640281-90-9  
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

CRN 57-03-4  
CMF C3 H9 O6 P

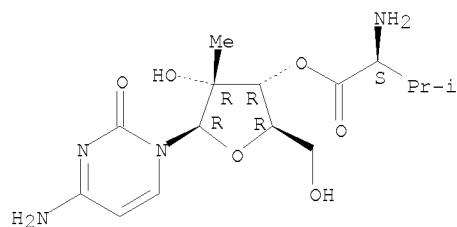


RN 642075-61-4 CAPLUS  
CN L-Valine, 3'-ester with 2'-C-methylcytidine, formate (salt) (9CI) (CA INDEX NAME)

CM 1

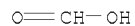
CRN 640281-90-9  
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

CRN 64-18-6  
CMF C H2 O2



RN 642075-62-5 CAPLUS  
CN L-Valine, 3'-ester with 2'-C-methylcytidine, (2E)-2-butenedioate (salt) (9CI) (CA INDEX NAME)

CM 1

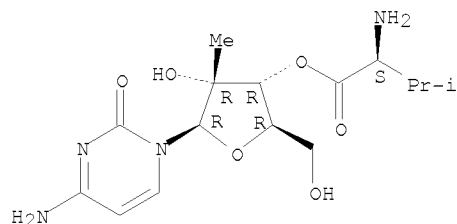
CRN 640281-90-9  
CMF C15 H24 N4 O6

McIntosh



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Absolute stereochemistry. Rotation (+).

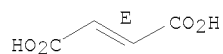


CM 2

CRN 110-17-8

CMF C4 H4 O4

Double bond geometry as shown.



RN 642075-63-6 CAPLUS

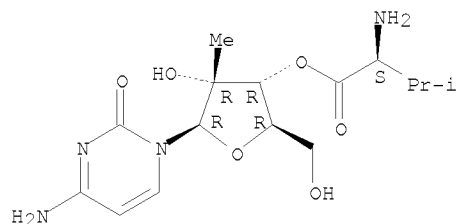
CN L-Valine, 3'-ester with 2'-C-methylcytidine, propanoate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

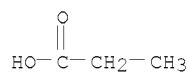
Absolute stereochemistry. Rotation (+).



CM 2

CRN 79-09-4

CMF C3 H6 O2



RN 642075-64-7 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydroxyacetate (salt) (9CI) (CA INDEX NAME)

CM 1

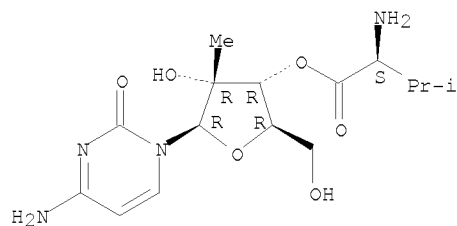
CRN 640281-90-9

CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).

McIntosh

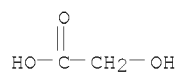
10/609,298



CM 2

CRN 79-14-1

CMF C2 H4 O3



RN 642075-65-8 CAPLUS

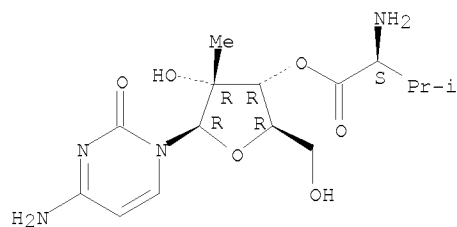
CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2-hydroxypropanoate (salt)  
(9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

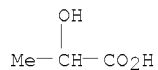
Absolute stereochemistry. Rotation (+).



CM 2

CRN 50-21-5

CMF C3 H6 O3



RN 642075-66-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2-oxopropanoate (salt) (9CI)  
(CA INDEX NAME)

CM 1

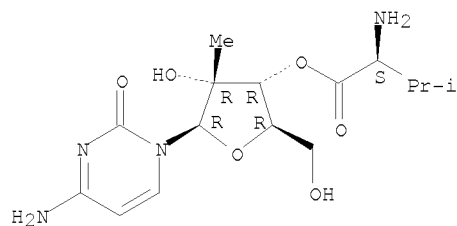
CRN 640281-90-9

CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).

McIntosh

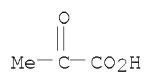
10/609,298



CM 2

CRN 127-17-3

CMF C3 H4 O3



RN 642075-67-0 CAPLUS

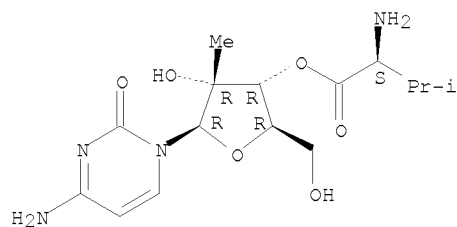
CN L-Valine, 3'-ester with 2'-C-methylcytidine, ethanedioate (salt) (9CI)  
(CA INDEX NAME)

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

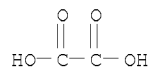
Absolute stereochemistry. Rotation (+).



CM 2

CRN 144-62-7

CMF C2 H2 O4



RN 642075-68-1 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, (2Z)-2-butenedioate (salt)  
(9CI) (CA INDEX NAME)

CM 1

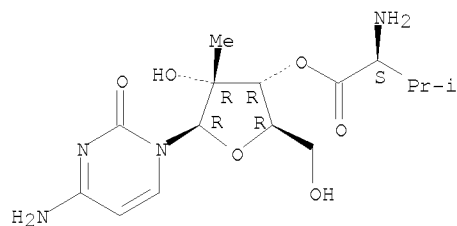
CRN 640281-90-9

CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).

McIntosh

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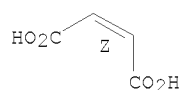


CM 2

CRN 110-16-7

CMF C4 H4 O4

Double bond geometry as shown.



RN 642075-69-2 CAPLUS

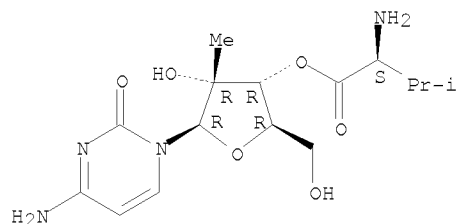
CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2-hydroxybenzoate (salt)  
(9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

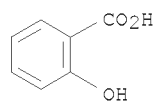
Absolute stereochemistry. Rotation (+).



CM 2

CRN 69-72-7

CMF C7 H6 O3



RN 642075-70-5 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, sulfate (salt) (9CI) (CA  
INDEX NAME)

CM 1

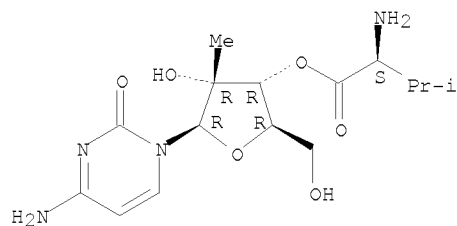
CRN 640281-90-9

CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).

McIntosh

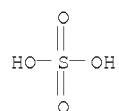
10/609,298



CM 2

CRN 7664-93-9

CMF H2 O4 S



RN 642075-71-6 CAPLUS

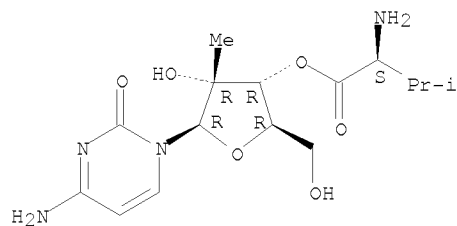
CN L-Valine, 3'-ester with 2'-C-methylcytidine, nitrate (salt) (9CI) (CA  
INDEX NAME)

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

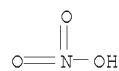
Absolute stereochemistry. Rotation (+).



CM 2

CRN 7697-37-2

CMF H N O3



RN 642075-72-7 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, carbonate (salt) (9CI) (CA  
INDEX NAME)

CM 1

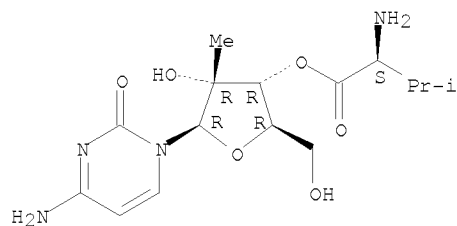
CRN 640281-90-9

CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).

McIntosh

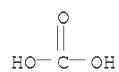
10/609,298



CM 2

CRN 463-79-6

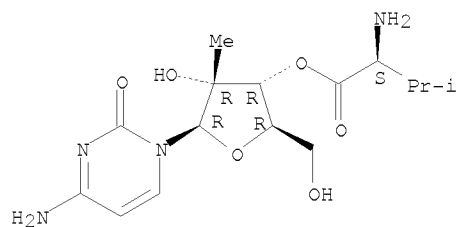
CMF C H2 O3



RN 642075-74-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrobromide (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

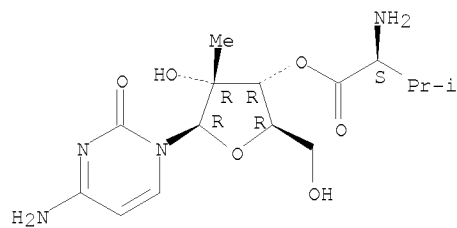


●x HBr

RN 642075-75-0 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydriodide (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



●x HI

RN 642075-76-1 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, carbonate (2:1) (salt) (9CI) (CA INDEX NAME)

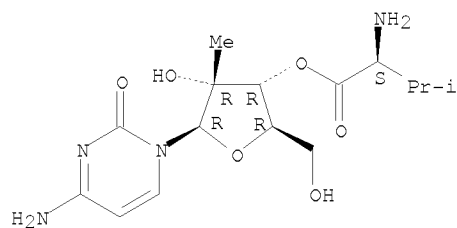
CM 1

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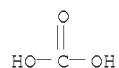
CRN 640281-90-9  
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

CRN 463-79-6  
CMF C H2 O3

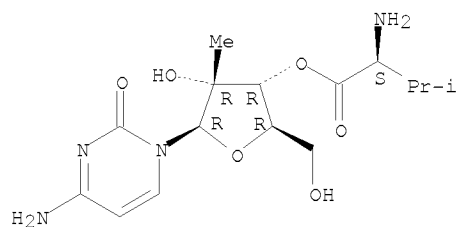


RN 642075-77-2 CAPLUS  
CN L-Valine, 3'-ester with 2'-C-methylcytidine, phosphate (salt) (9CI) (CA  
INDEX NAME)

CM 1

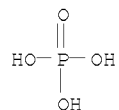
CRN 640281-90-9  
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

CRN 7664-38-2  
CMF H3 O4 P



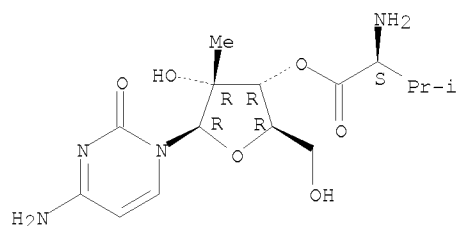
IT 640281-90-9P  
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT  
(Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use);  
BIOL (Biological study); PREP (Preparation); USES (Uses)  
(ribofuranosylcytidine methylvaline ester for treatment of  
flaviviridae infections)

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RN 640281-90-9 CAPLUS  
CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

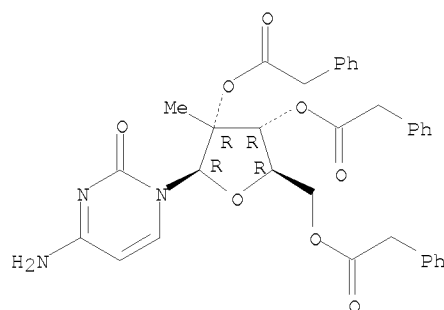
Absolute stereochemistry. Rotation (+).



IT 642075-41-0  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(ribofuranosylcytidine methylvaline ester for treatment of  
flaviviridae infections)

RN 642075-41-0 CAPLUS  
CN Cytidine, 2'-C-methyl-, 2',3',5'-tris(benzeneacetate) (9CI) (CA INDEX NAME)

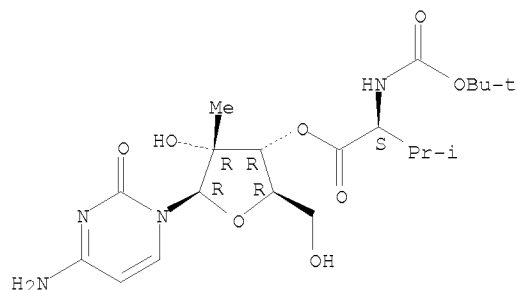
Absolute stereochemistry.



IT 640725-70-8P 642075-44-3P 642075-48-7P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(ribofuranosylcytidine methylvaline ester for treatment of  
flaviviridae infections)

RN 640725-70-8 CAPLUS  
CN L-Valine, N-[(1,1-dimethylethoxy)carbonyl]-, 3'-ester with  
2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry.



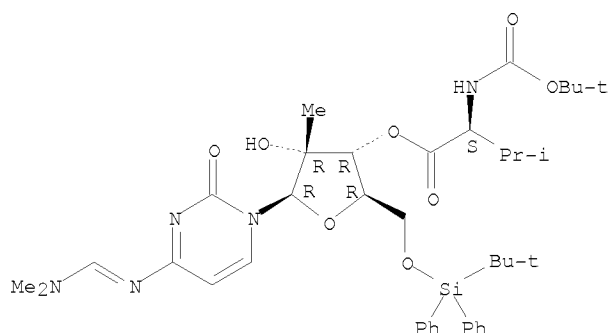
RN 642075-44-3 CAPLUS  
CN L-Valine, N-[(1,1-dimethylethoxy)carbonyl]-, 3'-ester with  
5'-O-[(1,1-dimethylethyl)diphenylsilyl]-N-[(dimethylamino)methylene]-2'-C-  
methylcytidine (CA INDEX NAME)

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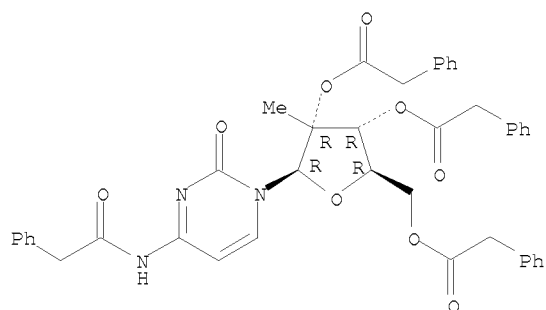
10/609,298

Absolute stereochemistry.  
Double bond geometry unknown.



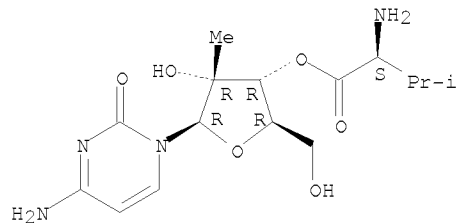
RN 642075-48-7 CAPLUS  
CN Cytidine, 2'-C-methyl-N-(phenylacetyl)-, 2',3',5'-tris(benzeneacetate)  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 640725-71-9P  
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(ribofuranosylcytidine methylvaline ester for treatment of flaviviridae infections)  
RN 640725-71-9 CAPLUS  
CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



● 2 HCl

=> d his

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(FILE 'HOME' ENTERED AT 18:07:49 ON 08 JUN 2008)

FILE 'REGISTRY' ENTERED AT 18:07:59 ON 08 JUN 2008

L1           STRUCTURE UPLOADED  
L2           24 S L1  
L3           519 S L1 FULL

FILE 'CAPLUS' ENTERED AT 18:08:46 ON 08 JUN 2008

L4           120 S L3  
L5           22498 S L4 AND FLAVIVIRUS OR PESTIVIRUS OR FLAVIVIRIDAE OR HCV OR HEP  
L6           58 S L4 AND (FLAVIVIRUS OR PESTIVIRUS OR FLAVIVIRIDAE OR HCV OR HE

FILE 'REGISTRY' ENTERED AT 18:13:47 ON 08 JUN 2008

L7           STRUCTURE UPLOADED  
L8           4 S L7  
L9           171 S L7 FULL

FILE 'CAPLUS' ENTERED AT 18:14:23 ON 08 JUN 2008

L10          74 S L9  
L11          37 S L10 AND (FLAVIVIRUS OR PESTIVIRUS OR FLAVIVIRIDAE OR HCV OR H